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REVIEWED
By Chris Tighe at 12:11 pm, Aug 15, 2018

CLASSES

First Generation Antipsychotics

BOXED WARNING

Dementia, geriatric, stroke

Use haloperidol with caution in the geriatric patient. The elderly are more prone to orthostatic hypotension and have greater sensitivity to anticholinergic effects. In addition, the elderly, particularly elderly females, may be more likely to develop extrapyramidal side effects, including tardive dyskinesia. Elderly patients may require lower initial doses of haloperidol, followed by careful titration. Antipsychotics such as haloperidol are not FDA approved for the treatment of dementia-related psychosis in geriatric patients and there is a boxed warning to this effect in the drug labels. Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Analyses of seventeen placebo-controlled trials (modal duration of 10 weeks), largely in patients taking atypical antipsychotic drugs, revealed a risk of death in drug-treated patients of between 1.6 to 1.7 times the risk of death in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature. Observational studies suggest that, similar to atypical antipsychotic drugs, treatment with conventional antipsychotic drugs may increase mortality. The extent to which the findings of increased mortality in observational studies may be attributed to the antipsychotic drug as opposed to some characteristic(s) of the patients is not clear. According to the Beers Criteria, antipsychotics are considered potentially inappropriate medications (PIMs) in elderly patients, and use should be avoided except for treating schizophrenia or bipolar disorder, and for short-term use as antiemetics during chemotherapy. In addition, avoidance of haloperidol is recommended in geriatric patients with the following disease states or symptoms due to the potential for exacerbation of the condition or increased risk of adverse effects: Parkinson's disease (symptom exacerbation), delirium (possible new-onset or worsening delirium), and dementia (adverse CNS effects). There is an increased risk of stroke and greater rate of cognitive decline and mortality in persons with dementia receiving antipsychotics, and the Beers expert panel recommends avoiding antipsychotics to treat delirium- or dementia-related behavioral problems unless non-pharmacological options have failed or are not possible and the patient is a substantial threat to self or others. The Panel recommends avoiding antipsychotics in elderly patients with a history of falls or fractures, unless safer alternatives are not available, since antipsychotics can cause ataxia, impaired psychomotor function, syncope, and additional falls; if an antipsychotic must be used, consider reducing use of other CNS-active medications that increase the risk of falls and fractures and implement other strategies to reduce fall risk. Because antipsychotics can cause or exacerbate hyponatremia and SIADH and the elderly are at increased risk of developing these conditions, sodium levels should be closely monitored when starting or changing dosages of antipsychotics in older adults. The federal Omnibus Budget Reconciliation Act (OBRA) regulates medication use in residents of long-term care facilities (LTCFs). An antipsychotic should generally be used only for the conditions listed in the guidelines (e.g., schizophrenia, mood disorder, Tourette's disorder) and that meet the Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria for use. There is an increased risk of morbidity and mortality in elderly patients treated with antipsychotics for dementia-related psychosis. Therefore, identify and address all possible causes of behavioral or psychological symptoms of dementia (BPSD) before considering an antipsychotic. To initiate antipsychotic therapy, behavioral symptoms must be a danger to self or others and are either 1) due to mania or psychosis or 2) the plan of care includes documentation of attempted behavioral interventions (except in an emergency). Limit emergency treatment to 7 days or less with evaluation and documentation within 7 days which identifies and addresses contributors/causes. For acute conditions persisting beyond 7 days, pertinent non-pharmacologic interventions must be attempted, unless clinically contraindicated, and documented. Treatment of non-acute, chronic, or prolonged BPSD must meet all of the OBRA criteria for BPSD treatment, and include monitoring that ensures the behavioral symptoms are not due to a treatable or correctable medical condition, are not due to correctable environmental or treatable psychological stressors alone, and provides clearly documented evidence of persistence. The LTCF must evaluate the appropriateness of the antipsychotic during or within 2 weeks of admission for a newly admitted resident on an antipsychotic. In all cases, the lowest possible dose and shortest duration should be prescribed. OBRA provides general dosing guidance for antipsychotic treatment of BPSD. Monitoring of antipsychotics should include evaluation of ongoing effectiveness, rationale for use, and potential adverse effects (e.g., anticholinergic effects, neurological symptoms, metabolic syndrome, cardiac effects). Antipsychotics are subject to periodic review for effectiveness, necessity, and the potential for gradual dose reduction (GDR) or discontinuation. Refer to the OBRA guidelines for complete information.

DEA CLASS

Rx

DESCRIPTION

High-potency oral and parenteral conventional antipsychotic structurally related to droperidol
Oral formulation and immediate-release intramuscular injection FDA-approved for treating schizophrenia and Tourette's Disorder; immediate-release IM formulation is effective for acute agitation in hospitalized settings
An intramuscular depot injection is available for schizophrenic patients requiring prolonged antipsychotic therapy
As with all antipsychotics, there is an increased risk of death in elderly patients treated for dementia-related psychosis; IV administration is not FDA-approved and is associated with an increased risk of QT prolongation and torsade de pointes (TdP)

COMMON BRAND NAMES

Haldol, Haldol Decanoate

HOW SUPPLIED

Haldol Decanoate/Haloperidol/Haloperidol Decanoate Intramuscular Inj Susp: 1mL, 50mg, 100mg
Haldol/Haloperidol Oral Tab: 0.5mg, 1mg, 2mg, 5mg, 10mg, 20mg

Haldol/Haloperidol/Haloperidol Lactate Intramuscular Inj Sol: 1mL, 5mg
Haloperidol/Haloperidol Lactate Oral Sol: 1mL, 2mg

DOSAGE & INDICATIONS

For the treatment of schizophrenia.

Oral dosage

Adults

Initially, 0.5 mg to 2 mg PO given 2 to 3 times per day in patients with moderate symptomatology or in debilitated patients. For severe, chronic, or refractory target symptoms, initiate with 3 to 5 mg PO given 2 to 3 times per day. Optimal response in geriatric patients is usually obtained with more gradual dosage adjustments and at lower dosages than what is required for younger adults. Adjust the dose based on response and tolerability. After the initial therapeutic response is achieved, slowly reduce to the lowest effective maintenance dose. The Patient Outcome Research Team (PORT) consensus guidelines recommend a dosage range for acute therapy of 6 mg/day to 20 mg/day and for maintenance therapy the PORT guidelines recommend a dosage range of 6 mg/day to 12 mg/day. Max: 100 mg/day PO.

Adolescents

0.5 to 5 mg/day PO; may administer in 2 or 3 divided doses. Although a pediatric dose for children and adolescents weighing more than 40 kg is not specified, FDA-approved labeling recommends 0.5 to 2 mg PO 2 to 3 times per day as an initial dose for adult patients with moderate symptomatology, or 3 to 5 mg PO 2 to 3 times per day for adult patients with severe, chronic, or treatment-resistant symptoms. Higher doses may be required in some cases to achieve prompt control. Patients who remain severely disturbed or inadequately controlled may require dosage adjustment. Max: 100 mg/day PO for severe refractory cases. After a therapeutic response is achieved, the dosage should be slowly reduced to the lowest effective maintenance dose.

Children 3 to 12 years and weighing 15 to 40 kg

0.5 mg/day PO initially; may administer in 2 or 3 divided doses. If clinically warranted, the dose may be increased by 0.5 mg increments at 5 to 7 day intervals until the desired therapeutic effect is obtained. The usual dose range is 0.05 mg/kg/day to 0.15 mg/kg/day PO; severe cases may require higher doses. A maximum effective dose has not been established; however, there is little evidence that behavior improvement is further enhanced with dosages above 6 mg/day PO. After a therapeutic response is achieved, the dosage should be slowly reduced to the lowest effective maintenance dose.

Intramuscular depot dosage (i.e., Haloperidol Decanoate depot injection)

Adults

Patients should be stabilized on an immediate-release antipsychotic before considering a conversion to haloperidol decanoate for treating schizophrenic patients who require prolonged parenteral therapy. In order to reduce the possibility of an unexpected adverse reaction to haloperidol decanoate, it is recommended that patients be treated with and tolerate short-acting haloperidol. ADULTS PREVIOUSLY MAINTAINED ON LOW ORAL DOSES OF ANTIPSYCHOTICS (E.G., UP TO THE EQUIVALENT OF 10 MG/DAY OF ORAL HALOPERIDOL) OR DEBILITATED ADULTS: The initial recommended IM depot dose is 10 to 15 times the previous antipsychotic dose in oral haloperidol equivalents, with subsequent adjustments based on response and tolerability. ADULTS PREVIOUSLY MAINTAINED ON HIGH ORAL DOSES OF ANTIPSYCHOTICS (E.G., GREATER THAN THE EQUIVALENT OF 10 MG/DAY OF HALOPERIDOL) FOR WHOM A LOW DOSE APPROACH RISKS DECOMPENSATION OR IN PATIENTS WHOSE LONG-TERM HALOPERIDOL USE HAS RESULTED IN TOLERANCE TO THE DRUG: The initial suggested IM depot dose is 20 times the previous antipsychotic dose in oral haloperidol equivalents, with downward titration on subsequent monthly doses. For all patients, the initial injection should not exceed 100 mg regardless of the previous antipsychotic dose requirements. If conversion requires an initial dose of more than 100 mg, the dose should be divided into 2 injections consisting of an initial injection not to exceed 100 mg followed by the balance in 3 to 7 days. The usual monthly maintenance range is 10 to 15 times the previous daily oral dose; however, the maintenance dosage should be titrated upward or downward based upon response and tolerability to reach the optimal regimen for each patient. The Patient Outcome Research Team (PORT) consensus guidelines recommend a maintenance dosage range of 50 mg to 200 mg every 4 weeks. With careful monitoring, haloperidol decanoate can be supplemented with oral haloperidol during dosage adjustments or symptom exacerbation. Usual Max: Clinical experience at doses greater than 450 mg/month IM has been limited.

Geriatric Adults

Patients should be stabilized on an immediate-release antipsychotic before considering a conversion to haloperidol decanoate for treating schizophrenic patients who require prolonged parenteral therapy. In order to reduce the possibility of an unexpected adverse reaction to haloperidol decanoate, it is recommended that patients be treated with and tolerate short-acting haloperidol. The initial and usual monthly IM maintenance dose range in geriatric patients is 10 to 15 times the previous antipsychotic dose in oral haloperidol equivalents, with titration upward or downward based on response and tolerability. The initial injection should not exceed 100 mg regardless of the previous antipsychotic dose requirements. If conversion requires an initial dose of more than 100 mg, the dose should be divided into 2 injections consisting of an initial injection not to exceed 100 mg followed by the balance in 3 to 7 days. The Patient Outcome Research Team (PORT) consensus guidelines recommend a maintenance dosage range of 50 mg to 200 mg every 4 weeks. With careful monitoring, haloperidol decanoate can be supplemented with oral haloperidol during dosage adjustments or symptom exacerbation. Usual Max: Clinical experience at doses greater than 450 mg/month IM has been limited.

For the treatment of severe behavioral problems associated with oppositional defiant disorder or other disruptive behavioral disorders, or for the treatment of attention-deficit hyperactivity disorder (ADHD) in pediatric patients who show excessive motor activity with accompanying conduct disorders.

Oral dosage

Children 3 to 12 years and weighing 15 to 40 kg

0.5 mg/day PO initially; may administer in 2 or 3 divided doses. If clinically warranted, the dose may be increased by 0.5 mg increments at 5 to 7 day intervals until the desired therapeutic effect is obtained. The usual dose range is 0.05 to 0.075 mg/kg/day PO. A maximum effective dose has not been established; however, there is little evidence that behavior improvement is further enhanced with dosages above 6 mg/day PO. Patients should be assessed periodically to determine the need for continued therapy; short-term treatment may be sufficient in some patients.

For the treatment of tics and vocal utterances associated with Tourette's syndrome.

Oral dosage

Adults

Initially, 0.5 to 2 mg PO given 2 to 3 times per day. Increase based on response. For severe, chronic or refractory target symptoms, 3 to 5 mg PO given 2 to 3 times per day. After therapeutic response is achieved, dosage should be slowly reduced according to patient tolerance and response. The average dose is approximately 15 mg/day PO. Max: 100 mg/day PO.

Adolescents

0.25 to 0.5 mg/day PO initially, slowly titrated by 0.25 to 0.5 mg increments at 5 to 7 day intervals until the desired therapeutic effect is obtained. The daily dosage may be given in 2 or 3 divided doses. Clinical guidelines suggest the usual dosage range is 1 mg/day to 4 mg/day PO. Max for those weighing 40 kg and less: 15 mg/day PO. Although a pediatric dose for adolescents weighing more than 40 kg is not specified, FDA-approved labeling recommends 0.5 to 2 mg PO 2 to 3 times per day as an initial dose for adult patients with moderate symptomatology, or 3 to 5 mg PO 2 to 3 times per day for adult patients with severe, chronic, or treatment-resistant symptoms; adult Max: 100 mg/day PO for severe refractory cases. After a therapeutic response is achieved, the dosage should be slowly reduced to the lowest effective maintenance dose.

Children 3 to 12 years and weighing 15 to 40 kg

0.25 to 0.5 mg/day PO initially, slowly titrated by 0.25 to 0.5 mg increments at 5 to 7 day intervals until the desired therapeutic effect is obtained. The daily dosage may be given in 2 or 3 divided doses. FDA approved labeling states the usual dose range is 0.05 to 0.075 mg/kg/day PO; this coincides closely with the usual dose range of 1 to 4 mg/day PO that clinical guidelines suggest. Max: 15 mg/day PO. After a therapeutic response is achieved, the dosage should be slowly reduced to the lowest effective maintenance dose.

For the treatment of acute agitation in patients with schizophrenia or an underlying psychiatric disorder.

For the treatment of acute agitation† in pediatric patients with an underlying psychiatric disorder.

Intramuscular dosage (haloperidol lactate injection)

Children† and Adolescents† 5 years and older

Controlled trials to establish the safety and effectiveness of IM dosing in pediatric patients for acute agitation secondary to psychiatric disorders have not been conducted. Off-label use is reported in the literature, but controlled trials are needed. IM dosing range: 0.025 mg/kg/dose to 0.075 mg/kg/dose (usually 2 to 5 mg per dose) IM as a single dose. Max per dose: 5 mg/dose IM has been recommended in some publications, though 10 mg/dose IM has been used in some patients. Repeat IM dosing is determined by symptom control, tolerance, and the ability to convert the patient to oral treatment as soon as feasible. Daily Max: Do not exceed 20 mg/day IM (usual adult max) in older pediatric patients.

Intramuscular dosage (i.e., haloperidol lactate injection)

Adults

2 to 5 mg IM single dose initially; use if oral therapy is not appropriate; may administer as frequently as 1 hour intervals, though dosing every 4 to 8 hours is satisfactory for most patients. Max: 20 mg/day IM. Repeat doses based on clinical response and safety considerations. Geriatric patients may require a lower dose; use lower starting dose and titrate gradually. Use the lowest effective dose in all patients. Convert to oral therapy as soon as clinically indicated. Second generation antipsychotics with efficacy for this indication (oral or parenteral, e.g., risperidone, olanzapine, or ziprasidone), may be preferred due to cardiac and extrapyramidal risks of parenteral haloperidol. In some patients, the addition of a benzodiazepine may be needed. SWITCHING TO ORAL THERAPY: In general, the parenteral dose administered in the preceding 24 hours may be used as the total initial daily PO dosage. Thereafter, closely monitor and adjust oral dosage to efficacy and tolerance. Usually, the first oral dose should be given within 12 to 24 hours following the last IM dose.

Intravenous dosage† (haloperidol lactate injection)

Adults

The intravenous route is not FDA approved and is generally not recommended except when no other alternatives are available. Intravenous administration appears to be associated with a higher risk of QT prolongation and torsade de pointes (TdP) than other forms of administration. The manufacturer recommends ECG monitoring for QT prolongation and arrhythmias if IV administration is required. A dose in the range of 1 to 5 mg IV has been suggested, with the dose being repeated at 30 to 60 minute intervals, if needed. A maximum IV dose has not been established. The lowest effective dose should be used in conjunction with conversion to oral therapy as soon as possible.

For the treatment of acute mania†.

Oral dosage

Adults

Doses of up to 10 mg to 25 mg PO every 4 to 6 hours have been recommended.

Intramuscular dosage (haloperidol lactate)

Adults

Doses of up to 5 mg to 10 mg IM every 4 to 6 hours have been recommended.

For the treatment of irritability associated with autistic disorder†.

Oral dosage

Children† and Adolescents† 3 years and older

Data are limited. In one small study of children 10 years and older, haloperidol was initiated at 0.25 mg/day PO at bedtime and titrated over 1 week to 0.5 mg twice daily. Thereafter, the dose was adjusted as clinically indicated. The mean daily dose was 1.3 mg and the range was 1 to 1.5 mg/day PO. In a separate study enrolling children 2.6 to 7.2 years of age, the optimal dose was 1.7 mg/day PO. Haloperidol was associated with significant improvement in withdrawal and stereotypy in children 4.5 years and older. Data from clinical trials assessing dyskinesias in young children (2 to 8 years of age) receiving long-term treatment (e.g., 6 months) with haloperidol indicate that tardive dyskinesia or withdrawal dyskinesias have occurred in approximately 20% to 34% of patients. The majority of cases have been withdrawal dyskinesias which were reversible. Due to the risk of extrapyramidal effects, haloperidol is generally reserved for children who have not responded to or are intolerant to therapy with an atypical antipsychotic.

For use as a second-line agent for rescue treatment of chemotherapy-induced nausea/vomiting†.

Intramuscular dosage (haloperidol lactate)

Adults

2 mg to 5 mg IM every 4 to 6 hours has been used as rescue treatment. Haldol is not a preferred agent due to the side effect profile; current guidelines specify the use of olanzapine as an alternative for breakthrough nausea/vomiting due to chemotherapy.

For the treatment of delirium† of patients in the intensive care unit.

For the treatment of delirium† in adults in the intensive care unit (ICU).

Oral dosage or Intramuscular dosage (haloperidol lactate)

Adults

The following have been recommended in the literature for adults. MILD AGITATION: Single doses of 0.5 to 2 mg PO or IM. Repeat doses should be based on clinical response. MODERATE AGITATION: Single doses of 5 to 10 mg PO or IM. Repeat doses are based on clinical response. SEVERE AGITATION: Single doses of 10 mg or more PO or IM. Repeat doses are based on clinical response.

Intravenous† dosage (haloperidol lactate)

Adults

The IV route has been used in critically ill patients; the best quality consensus reviews available recommend intermittent dosing; well controlled clinical trials are lacking. The usual initial dose is 2 mg to 10 mg IV. Many experts begin with a loading regimen of 2 mg IV, followed by repeat doses every 15 to 20 minutes while agitation persists. Thereafter once delirium is controlled, may repeat a dose every 4 to 6 hours, as needed, for a few days. Dosage reductions can be attempted, with tapering doses over several days. A typical taper regimen for the first day is one-half of the previous 24-hour total dose, given in divided doses. Haloperidol has been given occasionally as a continuous IV infusion (3 to 25 mg/hour IV); there are limited data to support infusions. Haloperidol lactate injection is not FDA-approved for intravenous (IV) administration. Cases of QT prolongation and torsade de pointes (TdP) have occurred, including fatalities, during IV use. ECG monitoring is recommended during IV administration. The risk increases with higher dosages (e.g., 20 mg/dose or more).

For the treatment of delirium† in the pediatric intensive care unit (PICU).

Intravenous dosage†

Children and Adolescents

Limited data available, particularly in young children. A loading dose of 0.15 to 0.25 mg IV given slowly over 30 to 45 minutes, followed by a maintenance dose of 0.05 to 0.5 mg/kg/24 hours IV (divided and given every 8 hours) has been described in several case reports/series (n = 39; age range: 3 months to 17 years). One small case series (n = 6; age range: 9 to 15 years) reported no loading dose but a modal individual maintenance dose of 0.5 mg IV. Maximum dose is unclear in pediatric patients; do not exceed 20 mg/day, the FDA-approved maximum parenteral dose in adults. Treatment of delirium often consisted of psychosocial, environmental, and, if warranted, pharmaceutical intervention. In general, IV haloperidol was reserved for patients with psychomotor agitation that was acutely threatening to their health. Pharmaceutical intervention lasted from a few hours to days and, in most cases, was stopped or tapered off during hospitalization or subsequently in an outpatient setting. Discontinue pharmacotherapy as soon as the acute phase of delirium has resolved. Haloperidol lactate injection is not FDA-approved for intravenous (IV) administration. Cases of QT prolongation and torsade de pointes (TdP) have occurred, including fatalities, during IV use. ECG monitoring is recommended during IV administration.

For the treatment of persistent singultus (hiccups)†.

Intramuscular dosage (haloperidol lactate)

Adults

2 mg to 5 mg IM has been effective in treating intractable hiccups from various causes. Haloperidol has less potential for producing hypotension as compared to chlorpromazine.

For the treatment of severe behavioral or psychological symptoms of dementia† (BPSD)†.

Oral dosage

Geriatric Adults

Initially, 0.25 mg or 0.5 mg PO 1 to 2 times per day. Increase by no more than 0.5 mg every 4 to 7 days if needed, in divided doses as necessary. Sedative effects may be minimized in some patients by using a single daily dose at bedtime. Antipsychotics are not FDA-approved for this indication and the labeling of all antipsychotics contains a boxed warning noting an increased risk of death in geriatric patients being treated for behavioral problems associated with dementia. The federal Omnibus Budget Reconciliation Act (OBRA) regulates the use of antipsychotics in long-term care facility (LTCF) residents with dementia-related behavioral symptoms. OBRA Max: 2 mg/day PO in residents meeting OBRA criteria for treatment, except when documentation is provided showing that higher doses are necessary to maintain or improve the resident's functional status. In addition, the facility must attempt a gradual dose reduction (GDR) in 2 separate quarters, at least 1 month apart, within the first year of admission to the facility or after the facility has initiated an antipsychotic, unless clinically contraindicated. After the first year, a GDR must be attempted annually unless clinically contraindicated. The GDR may be considered clinically contraindicated if the target symptoms returned or worsened after the most recent GDR attempt within the facility and the physician has documented justification for why attempting additional dose reductions at that time would likely impair the resident's function or increase distressed behavior.

†Indicates off-label use

MAXIMUM DOSAGE

Adults

100 mg/day PO. 20 mg/day IM of haloperidol lactate. Clinical experience with haloperidol decanoate doses greater than 450 mg/month IM is limited.

Geriatric

100 mg/day PO. 20 mg/day IM of haloperidol lactate. Clinical experience with haloperidol decanoate doses greater than 450 mg/month IM is limited.

Adolescents

weight more than 40 kg: 15 mg/day PO for Tourette's syndrome; there is no stated maximum dosage for adolescents with other indications; dosages exceeding 15 mg/day PO are rarely needed in adults but severely disturbed psychotic adults may require higher dosages; adult dosages up to 100 mg/day PO have been used in severe refractory cases. Safe and effective use of haloperidol injections has not been established (adult haloperidol lactate Max: 20 mg/day IM).
weight 40 kg or less: 0.15 mg/kg/day PO for most indications; severely psychotic patients may require higher doses (suggested Max: 6 mg/day PO for non-psychotic behaviors); 15 mg/day PO for Tourette's syndrome. Safe and effective use of haloperidol injections has not been established (adult haloperidol lactate Max: 20 mg/day IM).

Children

3 to 12 years and weight 15 to 40 kg: 0.15 mg/kg/day PO for most indications; severely psychotic children may require higher doses (suggested Max: 6 mg/day PO for non-psychotic behaviors); 15 mg/day PO for Tourette's syndrome. Safe and effective use of haloperidol injections has not been established (adult haloperidol lactate Max: 20 mg/day IM).
Less than 3 years or weight less than 15 kg: Safety and efficacy have not been established.

Infants

Safety and efficacy have not been established.

Neonates

Safety and efficacy have not been established.

DOSING CONSIDERATIONS

Hepatic Impairment

Specific guidelines for dosage adjustments in hepatic impairment are not available; however, reduced dosages or avoidance is advisable in patients with significant liver dysfunction. Haloperidol is extensively metabolized in the liver.

Renal Impairment

Specific guidelines for dosage adjustments in renal impairment are not available; it appears that no dosage adjustments are needed.

ADMINISTRATION

Oral Administration

May administer with food to minimize GI irritation.

Oral Liquid Formulations

Oral concentrate solution:
The concentrate can be administered directly from the calibrated pipette, or the solution can be mixed with a beverage or food prior to administration. However, the concentrate may precipitate if mixed with coffee or tea.
Avoid skin contact with solution during administration as contact dermatitis may occur.

Injectable Administration

Visually inspect parenteral products for particulate matter and discoloration prior to administration whenever solution and container permit.
Verify selection of proper injectable product prior to administration.

Instructions for opening injection ampules:
Lightly tap the top of the ampule until all of the fluid moves to the bottom of the ampule.
Hold the ampule between index finger and thumb with colored point (located at the base of the neck of the ampule) facing you.
Position index finger of the other hand to support the neck of the ampule. Position the thumb so that it covers the colored point and is parallel to the colored ring (located above the colored point).
Keeping the thumb on the colored point and with the index fingers close together, apply firm pressure on the colored point in the direction of the arrow to snap the ampule open.

Intravenous Administration

IV Push† (haloperidol lactate immediate-release injection solution only):
NOTE: IV administration of the lactate injection is not approved by the FDA in any population. Therefore, benefit to risk should be carefully assessed. Higher than recommended doses of any haloperidol formulation and IV administration appear to be associated with a higher risk of QT prolongation and torsade de pointes.
If haloperidol is administered IV, the ECG should be closely monitored for QT prolongation and arrhythmias.
SLOW IV push/infusion over several minutes is recommended to decrease the risk of hypotension, oversedation, extrapyramidal effects, and other adverse effects. Slow IV infusion over 30 to 45 minutes has also been reported for loading dose administration.
Carefully monitor efficacy and tolerability (sedation or other adverse effects) periodically for the first several days.
Switch to oral therapy, if needed, as soon as practical. When switching parenteral therapy to oral therapy, and depending on the patient’s clinical status, the first oral dose should be given within 12—24 hours following the last parenteral dose.

Intramuscular Administration

Haloperidol lactate immediate-release injection solution:
Administer by intramuscular (IM) injection.
Carefully monitor efficacy and tolerability (sedation or other adverse effects) periodically for the first several days.
The parenteral dose administered in the preceding 24 hours may be used to approximate the total daily dose required for subsequent parenteral treatment.
Switch to oral therapy, if needed, as soon as practical. When switching parenteral therapy to oral therapy, and depending on the patient’s clinical status, the first oral dose should be given within 12—24 hours following the last parenteral dose.

Haloperidol decanoate depot injection in oil:
Do NOT administer intravenously. Administer by deep intramuscular (IM) injection ONLY.
The volume per injection site should not exceed 3 mL.
A 21 gauge needle is recommended.

STORAGE

Generic:
- Protect from freezing
- Protect from light
- Store at controlled room temperature (between 68 and 77 degrees F)
Haldol:
- Do not freeze
- Protect from light

- Store at controlled room temperature (between 68 and 77 degrees F)
Haldol Decanoate:
- Discard product if it contains particulate matter, is cloudy, or discolored
- Do not freeze
- Do not refrigerate
- Protect from light
- Store at controlled room temperature (between 68 and 77 degrees F)
- Store in carton until contents are used

CONTRAINDICATIONS / PRECAUTIONS

General Information

Haloperidol is contraindicated in patients with a known haloperidol hypersensitivity or hypersensitivity to components of the specific formulation used.

Alcoholism, angina, bradycardia, cardiac arrhythmias, cardiac disease, coronary artery disease, diabetes mellitus, females, heart failure, hypertension, hypocalcemia, hypokalemia, hypomagnesemia, hypotension, intravenous administration, long QT syndrome, malnutrition, myocardial infarction, orthostatic hypotension, QT prolongation, thyroid disease, torsade de pointes

Haloperidol decanoate is for intramuscular use only and must not be given by intravenous administration. Haloperidol lactate injection is not FDA approved for intravenous administration. However, clinically, haloperidol lactate has been used for control of acute agitation or related behavioral symptoms, particularly in the intensive care setting. According to the FDA, at least 28 cases of QT prolongation and torsade de pointes (TdP) have been documented in the medical literature. These events appear to be dose-related and have frequently occurred in association with higher than recommended dosages or during intravenous (IV) administration. Fatalities have been reported in some cases involving IV use of the drug. Due to the severity of these cardiac events, ECG monitoring is recommended during IV administration. The use of haloperidol decanoate has also been associated with TdP, QT prolongation, ventricular arrhythmias, and sudden death. Use haloperidol with caution in patients with cardiac disease or other conditions that may increase the risk of QT prolongation including cardiac arrhythmias, congenital long QT syndrome, heart failure, bradycardia, myocardial infarction, hypertension, coronary artery disease, hypomagnesemia, hypokalemia, hypocalcemia, or in patients receiving medications known to prolong the QT interval or cause electrolyte imbalances. Females, elderly patients, patients with diabetes mellitus, thyroid disease, malnutrition, alcoholism, or hepatic impairment may also be at increased risk for QT prolongation. Haloperidol administration has also been associated with transient hypotension and precipitation of angina; use caution in patients with preexisting hypotension or angina. Antipsychotics may cause orthostatic hypotension, which could lead to falls with the potential for fractures and other injuries. A fall risk assessment should be completed when initiating an antipsychotic in patients with conditions, diseases, or concurrent medication use that could exacerbate orthostasis. A fall risk assessment should be completed recurrently in at-risk patients on long-term antipsychotic therapy.

Agranulocytosis, hematological disease, leukopenia, neutropenia

Haloperidol should be used with caution in patients with hematological disease. Hematologic effects including leukopenia, neutropenia, and agranulocytosis have been associated with antipsychotic use. A history of drug-induced leukopenia or neutropenia or pre-existing low white blood cell (WBC) count may increase the likelihood of developing hematologic effects during treatment with an antipsychotic medication. Patients with a history of clinically significant low WBC count or drug-induced leukopenia/neutropenia should have frequent complete blood count (CBC) assessments during the first few months of treatment. Discontinuation of the antipsychotic should be considered if a clinically significant decline in WBC occurs in the absence of an identifiable cause. Patients with clinically significant neutropenia should be closely monitored for fever and infection, and appropriate medical intervention should be instituted if necessary. Haloperidol should be discontinued in patients with severe neutropenia (ANC less than 1,000/mm3); ongoing medical care is recommended until the symptoms resolve.

CNS depression, coma

Haloperidol is contraindicated in patients who are in a coma or who exhibit severe toxic CNS depression. Severe adverse CNS reactions induced by haloperidol may appear similar to neurologic symptoms of CNS disorders such as encephalitis, Reye's syndrome, encephalopathy, meningitis, and tetanus.

Tardive dyskinesia

Tardive dyskinesia is a syndrome of potentially irreversible, involuntary, dyskinetic movements that may develop in patients treated with antipsychotics. Periodic evaluation for movement disorders is recommended (e.g., AIMS). Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is impossible to rely upon prevalence estimates to predict, at the initiation of antipsychotic treatment, which patients are likely to develop the syndrome. Whether antipsychotics differ in their potential to cause tardive dyskinesia is unknown. The risk of developing tardive dyskinesia and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotics administered to the patient increase. However, the syndrome can develop, although much less commonly, after relatively brief periods at low doses or may even arise after drug discontinuation. The syndrome may remit, partially or completely, if the antipsychotic is withdrawn. Antipsychotics may suppress (or partially suppress) the signs and symptoms of the syndrome and thereby may possibly mask the underlying process. The effect that symptomatic suppression has upon the long-term course of the syndrome is unknown. Given these considerations, haloperidol should be prescribed in a manner that is most likely to minimize the occurrence of tardive dyskinesia. Chronic antipsychotic treatment should generally be reserved for patients who suffer from a chronic illness that is known to respond to antipsychotics, and for whom alternative, equally effective, but potentially less harmful treatments are not available or appropriate. In patients who do require chronic therapy, the smallest dose and the shortest duration producing a satisfactory clinical response should be sought. The need for continued treatment should be reassessed periodically. If signs and symptoms of tardive dyskinesia appear, haloperidol discontinuation should be considered. However, some patients may require treatment despite the presence of the syndrome.

Neurological disease, Parkinson's disease

Antipsychotics can cause motor and sensory instability, which may lead to falls with the potential for fractures and other injuries. A fall risk assessment should be completed when initiating an antipsychotic in patients with diseases (e.g., neurological disease), conditions, or concurrent medication use that could exacerbate motor and sensory instability. A fall risk assessment should be completed recurrently in at-risk patients on long-term antipsychotic therapy. Haloperidol is contraindicated in patients with Parkinson's disease. The dopamine blockade from haloperidol may dramatically worsen the preexisting Parkinson's disease, possibly incapacitating the patient. Atypical antipsychotics are less likely to interfere with treatments for Parkinson's disease than traditional antipsychotic agents like haloperidol. In general, avoid traditional antipsychotic use during therapy for Parkinson's disease unless the benefit of the drug outweighs the risk of decreased therapeutic response to levodopa or other treatments.

Coadministration with other CNS depressants, driving or operating machinery, ethanol ingestion

Haloperidol can cause somnolence. Somnolence could lead to falls with the potential for fractures and other injuries. A fall risk assessment should be completed when initiating an antipsychotic in patients with conditions, diseases, or concurrent medication use that could exacerbate somnolence. A fall risk assessment should be completed recurrently in at-risk patients on long-term antipsychotic therapy. Patients receiving haloperidol should

be advised to avoid driving or operating machinery until the effects of the drug are known. Given the primary CNS effects of haloperidol, caution should be used during coadministration with other CNS depressants and alcohol. Ethanol ingestion may further impair cognitive and motor skills and patients should be advised to avoid use of alcoholic beverages.

Seizure disorder, seizures

Patients with a seizure disorder, history of seizures, or electroencephalogram (EEG) abnormalities should be monitored carefully during therapy with haloperidol because antipsychotics can lower the seizure threshold. High doses and rapid dose changes should be avoided in patients with a known history of seizures.

Dysphagia

Patients with dysphagia or who are at risk for aspiration should be closely monitored while receiving haloperidol. Antipsychotics have been associated with esophageal dysmotility and aspiration of gastric contents, which may increase the incidence of aspiration pneumonia in susceptible patient populations.

Pulmonary disease

Because of potential effects on respiration, haloperidol should be used with caution in patients with pulmonary disease. Several cases of bronchopneumonia, some fatal, have followed the use of antipsychotic drugs, including haloperidol, and the infection risk may result from hemoconcentration, reduced pulmonary ventilation, and the dehydrated state that are secondary to decreased thirst and lethargy due to CNS depression. If signs and symptoms of pneumonia develop, especially in the elderly, an evaluation should be promptly initiated.

Hepatic disease, jaundice

Haloperidol is extensively metabolized in the liver and should be used with caution in patients with pre-existing hepatic disease. Lower initial doses and slower titration are advisable; however, specific guidelines are not available. Liver impairment in the form of cholestasis with jaundice has been reported rarely with administration of haloperidol.

Closed-angle glaucoma, increased intraocular pressure, visual disturbance

Evaluate patients who complain of unusual visual disturbance. Although not reported with haloperidol, decreased serum cholesterol and/or cutaneous and ocular changes have been reported in patients receiving chemically-related drugs. The anticholinergic effects of haloperidol are minimal; however, concomitant use of anticholinergic drugs (e.g., benztropine) to treat extrapyramidal symptoms may increase the likelihood of increased intraocular pressure or closed-angle glaucoma.

Prostatic hypertrophy, urinary retention

Haloperidol should be used cautiously in patients with prostatic hypertrophy. The anticholinergic effects of haloperidol are minimal. However, haloperidol has been reported to cause urinary retention, which may be more likely to occur in susceptible individuals. Co-use of an anticholinergic medication (e.g., benztropine) to treat extrapyramidal symptoms with haloperidol may increase the risk for urinary retention.

Dementia, geriatric, stroke

Use haloperidol with caution in the geriatric patient. The elderly are more prone to orthostatic hypotension and have greater sensitivity to anticholinergic effects. In addition, the elderly, particularly elderly females, may be more likely to develop extrapyramidal side effects, including tardive dyskinesia. Elderly patients may require lower initial doses of haloperidol, followed by careful titration. Antipsychotics such as haloperidol are not FDA approved for the treatment of dementia-related psychosis in geriatric patients and there is a boxed warning to this effect in the drug labels. Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Analyses of seventeen placebo-controlled trials (modal duration of 10 weeks), largely in patients taking atypical antipsychotic drugs, revealed a risk of death in drug-treated patients of between 1.6 to 1.7 times the risk of death in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature. Observational studies suggest that, similar to atypical antipsychotic drugs, treatment with conventional antipsychotic drugs may increase mortality. The extent to which the findings of increased mortality in observational studies may be attributed to the antipsychotic drug as opposed to some characteristic(s) of the patients is not clear. According to the Beers Criteria, antipsychotics are considered potentially inappropriate medications (PIMs) in elderly patients, and use should be avoided except for treating schizophrenia or bipolar disorder, and for short-term use as antiemetics during chemotherapy. In addition, avoidance of haloperidol is recommended in geriatric patients with the following disease states or symptoms due to the potential for exacerbation of the condition or increased risk of adverse effects: Parkinson's disease (symptom exacerbation), delirium (possible new-onset or worsening delirium), and dementia (adverse CNS effects). There is an increased risk of stroke and greater rate of cognitive decline and mortality in persons with dementia receiving antipsychotics, and the Beers expert panel recommends avoiding antipsychotics to treat delirium- or dementia-related behavioral problems unless non-pharmacological options have failed or are not possible and the patient is a substantial threat to self or others. The Panel recommends avoiding antipsychotics in elderly patients with a history of falls or fractures, unless safer alternatives are not available, since antipsychotics can cause ataxia, impaired psychomotor function, syncope, and additional falls; if an antipsychotic must be used, consider reducing use of other CNS-active medications that increase the risk of falls and fractures and implement other strategies to reduce fall risk. Because antipsychotics can cause or exacerbate hyponatremia and SIADH and the elderly are at increased risk of developing these conditions, sodium levels should be closely monitored when starting or changing dosages of antipsychotics in older adults. The federal Omnibus Budget Reconciliation Act (OBRA) regulates medication use in residents of long-term care facilities (LTCFs). An antipsychotic should generally be used only for the conditions listed in the guidelines (e.g., schizophrenia, mood disorder, Tourette's disorder) and that meet the Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria for use. There is an increased risk of morbidity and mortality in elderly patients treated with antipsychotics for dementia-related psychosis. Therefore, identify and address all possible causes of behavioral or psychological symptoms of dementia (BPSD) before considering an antipsychotic. To initiate antipsychotic therapy, behavioral symptoms must be a danger to self or others and are either 1) due to mania or psychosis or 2) the plan of care includes documentation of attempted behavioral interventions (except in an emergency). Limit emergency treatment to 7 days or less with evaluation and documentation within 7 days which identifies and addresses contributors/causes. For acute conditions persisting beyond 7 days, pertinent non-pharmacologic interventions must be attempted, unless clinically contraindicated, and documented. Treatment of non-acute, chronic, or prolonged BPSD must meet all of the OBRA criteria for BPSD treatment, and include monitoring that ensures the behavioral symptoms are not due to a treatable or correctable medical condition, are not due to correctable environmental or treatable psychological stressors alone, and provides clearly documented evidence of persistence. The LTCF must evaluate the appropriateness of the antipsychotic during or within 2 weeks of admission for a newly admitted resident on an antipsychotic. In all cases, the lowest possible dose and shortest duration should be prescribed. OBRA provides general dosing guidance for antipsychotic treatment of BPSD. Monitoring of antipsychotics should include evaluation of ongoing effectiveness, rationale for use, and potential adverse effects (e.g., anticholinergic effects, neurological symptoms, metabolic syndrome, cardiac effects). Antipsychotics are subject to periodic review for effectiveness, necessity, and the potential for gradual dose reduction (GDR) or discontinuation. Refer to the OBRA guidelines for complete information.

Thyrotoxicosis

Severe neurotoxicity (rigidity, inability to walk or talk) may occur in patients with thyrotoxicosis who are receiving an antipsychotic agent such as haloperidol.

Ambient temperature increase, dehydration, hyperthermia, hypothermia, strenuous exercise

Antipsychotics have been reported to disrupt the body's ability to reduce core body temperature presumably through effects in the hypothalamus, and they predispose patients to hyperthermia. Patients receiving haloperidol should be advised of conditions that contribute to an elevation in core body temperature (e.g., strenuous exercise, ambient temperature increase, or dehydration). A less frequently described alteration in thermoregulatory processes reported with both conventional and atypical antipsychotics is hypothermia. Thermoregulation is multi-factorial; however, the dopaminergic system appears to have a primary role, and serotonin may also have modulatory activity (5-HT2a receptors). Most cases of hypothermia associated with antipsychotics have occurred in conjunction with other potential precipitating factors such as hypothyroidism, sepsis, organic brain injury, or environmental temperature. Hypothermia appears to occur more frequently during initiation of antipsychotic therapy or after dose increases.

Tobacco smoking

Tobacco smoke contains polycyclic aromatic hydrocarbons that induce hepatic cytochrome P450 (CYP450) microsomal enzymes. There is some evidence to suggest that tobacco smoking accelerates the metabolism of haloperidol. Because the effect on hepatic microsomal enzymes is not related to the nicotine component of tobacco, the sudden cessation of tobacco smoking may result in a reduced clearance of haloperidol, despite the initiation of a nicotine replacement product. Monitor patients carefully when changes in smoking status occur.

Abrupt discontinuation

In general, short-term antipsychotic therapy is not associated with symptoms related to abrupt discontinuation; however, some patients on maintenance treatment experience transient dyskinetic signs after abrupt withdrawal. In some cases, the dyskinetic movements are not distinguishable from tardive dyskinesia except for duration. It is not known if a gradual taper reduces the rate of withdrawal-emergent neurological signs, but until further evidence becomes available, it is reasonable to gradually withdraw haloperidol when clinically feasible. Other discontinuation symptoms that have been reported with abrupt discontinuation of antipsychotics include nausea, vomiting, anorexia, diaphoresis, headache, insomnia, restlessness, anxiety and agitation.

Breast cancer, hyperprolactinemia, infertility

Close monitoring for adverse endocrine effects is advisable during haloperidol administration. Antipsychotics can cause hyperprolactinemia, likely due to central dopamine antagonism. Elevations in prolactin may result in infertility in either men or women. Some hyperprolactinemic women with normal menstruation may have an increased number of anovulatory cycles, which may result in subfertility. Hyperprolactinemia may also result in galactorrhea, amenorrhea, gynecomastia, impotence, or other genitourinary effects. Chronic hyperprolactinemia when associated with hypogonadism may lead to decreased bone density in males or females. In vitro data indicate that about one-third of human breast cancers may be prolactin-dependent; therefore, haloperidol should be used cautiously in those who have a history of breast cancer. It should be noted that neither clinical trials nor epidemiologic studies conducted to date have shown an association between chronic administration of antipsychotics and mammary tumorigenesis in humans, but the available evidence is too limited to be conclusive.

Neonates, pregnancy, pregnancy testing

Haloperidol should be used during human pregnancy only when the benefits to the mother outweigh the potential risks to the fetus. No well-controlled data are available to determine the safety and efficacy of haloperidol use during human pregnancy. Neonates exposed to antipsychotics during the third trimester of pregnancy are at risk for extrapyramidal and/or withdrawal symptoms following delivery. There have been reports of agitation, hypertonia, hypotonia, tremor, somnolence, respiratory distress and feeding disorder in these neonates. These complications have varied in severity and have ranged from self-limited to those requiring intensive care unit support and prolonged hospitalization. Neonates exhibiting signs or symptoms of extrapyramidal effects or withdrawal should be carefully monitored. In one prospective cohort study, the rate of major anomalies after fetal exposure to haloperidol or the related compound penfluridol during pregnancy was assessed. In this study, pregnant women who contacted the European Network of Teratology Information Services (ENTIS) for counseling in regard to gestational exposure to haloperidol or penfluridol were followed and compared to an ENTIS control group of women who had been counseled during pregnancy in regard to non-teratogenic exposures. Over a 13-year period, the rate of congenital anomalies did not differ between the haloperidol/penfluridol group (n = 188/27 respectively) and the control group (n = 631), nor were there differences during a separate analysis of first trimester exposure. However, there were 2 cases of limb defects in the haloperidol/penfluridol group and none in the control group. A separate study evaluated the maternal use of antipsychotics in early pregnancy and during delivery by analyzing data from the Swedish Medical Birth Registry. Of the 79 infants exposed to butyrophenone derivatives (e.g., haloperidol, melperone), there was 1 severe case of microphthalmia combined with gastroschisis and 1 case of renal dysplasia and pes equinovarus. The knowledge about long-term neurobehavioral effects in offspring is limited for all antipsychotic agents and requires further investigation. According to the American Psychiatric Association treatment guidelines for schizophrenia, consider pregnancy testing in women of childbearing potential prior to initiation of an antipsychotic. The National Pregnancy Registry for Psychiatric Medications is dedicated to evaluating the safety of psychiatric medications that may be taken by women during pregnancy to treat a wide range of mood, anxiety, or psychiatric disorders. The primary goal of this Registry is to determine the frequency of major malformations, such as heart defects, cleft lip, or neural tube defects, in babies exposed to various psychiatric drugs during pregnancy. While the research concentrates on atypical antipsychotics and antidepressant use, pregnant women using other psychiatric medications are encouraged to register. For more information, contact the registry at https://womensmentalhealth.org/clinical-and-research-programs/pregnancyregistry or by phone 1-866-961-2388. It is not known if antipsychotics, through their effect on prolactin, would affect labor or obstetric delivery.

Breast-feeding

According to the manufacturers of the oral and injectable formulations, breast-feeding should be avoided during treatment with haloperidol. Haloperidol is excreted into breast milk. In one small study, developmental delays were reported in some nursing infants following combined use of haloperidol and chlorpromazine, while monotherapy did not result in this outcome. Conversely, in 2 women who received 5 mg/day of haloperidol plus olanzapine or amisulpride during pregnancy and breast-feeding, the breastfed infants exhibited normal development, and no adverse effects were noted during the 11 to 13 month follow-up period. In other case reports of breast-feeding during haloperidol monotherapy or combination therapy with imipramine or trihexyphenidyl and a haloperidol dose in the general range of 7.5 mg/day to 15 mg/day, age-appropriate development of the breastfed infants occurred during the follow-up period (range: 12 months to 8 years). Haloperidol may cause elevated prolactin levels and galactorrhea, and thus has the potential to alter proper lactation in some patients. Some data suggest that postnatal women are more sensitive to the prolactin-elevating effects of antipsychotics than nonpuerperal women. Due to individual variability in response to antipsychotics, it may be prudent to continue the existing regimen if ongoing treatment is deemed necessary during breast-feeding; however, alternate medications for consideration include atypical agents such as olanzapine or quetiapine. Data regarding the safety of atypical antipsychotics during breast-feeding are limited and chronic administration of any antipsychotic during breast-feeding should be avoided if possible. Regardless of the antipsychotic used, the nursing infant should be closely monitored for excessive drowsiness, lethargy, and developmental delays. Combination treatment with antipsychotics may increase the risk of these adverse events. Consider the benefits of breast-feeding, the risk of potential infant drug exposure, and the risk of an untreated or inadequately treated condition. If a breast-feeding infant experiences an adverse effect related to a maternally ingested drug, healthcare providers are encouraged to report adverse effects to the FDA.

ADVERSE REACTIONS

Severe

seizures / Delayed / 0-1.0
akinesia / Delayed / 2.8
torticollis / Delayed / Incidence not known

tardive dyskinesia / Delayed / Incidence not known
agranulocytosis / Delayed / Incidence not known
pancytopenia / Delayed / Incidence not known
hemolytic anemia / Delayed / Incidence not known
aplastic anemia / Delayed / Incidence not known
retinopathy / Delayed / Incidence not known
visual impairment / Early / Incidence not known
hepatic failure / Delayed / Incidence not known
exfoliative dermatitis / Delayed / Incidence not known
vasculitis / Delayed / Incidence not known
anaphylactoid reactions / Rapid / Incidence not known
stroke / Early / Incidence not known
torsade de pointes / Rapid / Incidence not known
ventricular tachycardia / Early / Incidence not known
cardiac arrest / Early / Incidence not known
ventricular fibrillation / Early / Incidence not known
laryngeal edema / Rapid / Incidence not known
laryngospasm / Rapid / Incidence not known
bronchospasm / Rapid / Incidence not known
SIADH / Delayed / Incidence not known
water intoxication / Delayed / Incidence not known
neuroleptic malignant syndrome / Delayed / Incidence not known
rhabdomyolysis / Delayed / Incidence not known
neonatal abstinence syndrome / Early / Incidence not known

Moderate

constipation / Delayed / 1.0-10.0
hallucinations / Early / 0-1.0
akathisia / Delayed / 10.0
hypertonia / Delayed / 10.0
pseudoparkinsonism / Delayed / 10.0
dystonic reaction / Delayed / 10.0
dyskinesia / Delayed / Incidence not known
trismus / Delayed / Incidence not known
nystagmus / Delayed / Incidence not known
euphoria / Early / Incidence not known
confusion / Early / Incidence not known
depression / Delayed / Incidence not known
anemia / Delayed / Incidence not known
neutropenia / Delayed / Incidence not known
leukopenia / Delayed / Incidence not known
eosinophilia / Delayed / Incidence not known
thrombocytopenia / Delayed / Incidence not known
hyperprolactinemia / Delayed / Incidence not known
priapism / Early / Incidence not known
ejaculation dysfunction / Delayed / Incidence not known
osteopenia / Delayed / Incidence not known
galactorrhea / Delayed / Incidence not known
infertility / Delayed / Incidence not known
urinary retention / Early / Incidence not known
impotence (erectile dysfunction) / Delayed / Incidence not known
blurred vision / Early / Incidence not known
cataracts / Delayed / Incidence not known
dysphagia / Delayed / Incidence not known
cholestasis / Delayed / Incidence not known
jaundice / Delayed / Incidence not known
hepatitis / Delayed / Incidence not known
elevated hepatic enzymes / Delayed / Incidence not known
contact dermatitis / Delayed / Incidence not known
edema / Delayed / Incidence not known
QT prolongation / Rapid / Incidence not known
sinus tachycardia / Rapid / Incidence not known
hypotension / Rapid / Incidence not known
orthostatic hypotension / Delayed / Incidence not known
dyspnea / Early / Incidence not known
hyponatremia / Delayed / Incidence not known
heat intolerance / Early / Incidence not known
hyperthermia / Delayed / Incidence not known
withdrawal / Early / Incidence not known
hypoglycemia / Early / Incidence not known
hyperglycemia / Delayed / Incidence not known
hyperammonemia / Delayed / Incidence not known

Mild

xerostomia / Early / 1.0-10.0
drowsiness / Early / 5.3-5.3
headache / Early / 2.8-2.8
abdominal pain / Early / 2.8-2.8
hypersalivation / Early / 1.2-1.2
tremor / Early / 10.0
hyperkinesis / Delayed / 10.0
lethargy / Early / 10.0
restlessness / Early / 10.0
weight gain / Delayed / 10.0
anxiety / Delayed / Incidence not known

agitation / Early / Incidence not known
insomnia / Early / Incidence not known
vertigo / Early / Incidence not known
purpura / Delayed / Incidence not known
fever / Early / Incidence not known
menorrhagia / Delayed / Incidence not known
mastalgia / Delayed / Incidence not known
amenorrhea / Delayed / Incidence not known
menstrual irregularity / Delayed / Incidence not known
gynecomastia / Delayed / Incidence not known
libido decrease / Delayed / Incidence not known
dysmenorrhea / Delayed / Incidence not known
retinal pigment changes / Delayed / Incidence not known
weight loss / Delayed / Incidence not known
nausea / Early / Incidence not known
vomiting / Early / Incidence not known
rash / Early / Incidence not known
pruritus / Rapid / Incidence not known
acneiform rash / Delayed / Incidence not known
photosensitivity / Delayed / Incidence not known
hyperhidrosis / Delayed / Incidence not known
urticaria / Rapid / Incidence not known
injection site reaction / Rapid / Incidence not known
polydipsia / Early / Incidence not known
hypothermia / Delayed / Incidence not known

DRUG INTERACTIONS

Abarelix: (Severe) Since abarelix can cause QT prolongation, abarelix should be used cautiously, if at all, with other drugs that are associated with QT prolongation including haloperidol. Prescribers need to weigh the potential benefits and risks of abarelix use in patients that are taking drugs that can cause QT prolongation.
Abiraterone: (Moderate) Monitor for an increase in haloperidol-related adverse reactions if coadministration with abiraterone is necessary. Haloperidol is a CYP2D6 substrate and abiraterone is a moderate CYP2D6 inhibitor. In pharmacokinetic studies, mild to moderately increased haloperidol concentrations have been reported when haloperidol was given concomitantly with drugs characterized as inhibitors of CYP2D6.
Acebutolol: (Moderate) Haloperidol should be used cautiously with acebutolol due to the possibility of additive hypotension.
Acetaminophen; Butalbital: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as barbiturates. Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.
Acetaminophen; Butalbital; Caffeine: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as barbiturates. Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.
Acetaminophen; Butalbital; Caffeine; Codeine: (Moderate) Concomitant use of codeine with haloperidol may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. It is recommended to avoid this combination when codeine is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of haloperidol could decrease codeine plasma concentrations and increase morphine plasma concentrations resulting in prolonged opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. If haloperidol is discontinued, monitor the patient carefully and consider reducing the opioid dosage if appropriate. Codeine is primarily metabolized by CYP2D6 to morphine, and by CYP3A4 to norcodeine; norcodeine does not have analgesic properties. Haloperidol is a moderate inhibitor of CYP2D6. (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as barbiturates. Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.
Acetaminophen; Caffeine; Dihydrocodeine: (Moderate) Concomitant use of a potent CYP2D6 inhibitor like haloperidol with dihydrocodeine-containing products may decrease the metabolism of dihydrocodeine to dihydromorphine. Although theoretical, patients may experience varying degrees of analgesia if they take dihydrocodeine with a CYP2D6 inhibitor.
Acetaminophen; Chlorpheniramine; Dextromethorphan; Phenylephrine: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol, directly counteract the effects of phenylephrine and can counter the desired pharmacologic effect. They also can be used to treat excessive phenylephrine-induced hypertension.
Acetaminophen; Chlorpheniramine; Dextromethorphan; Pseudoephedrine: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol directly counteract the effects of pseudoephedrine and can counter the desired pharmacologic effect. They also can be used to treat excessive pseudoephedrine-induced hypertension.
Acetaminophen; Chlorpheniramine; Phenylephrine; Phenyltoloxamine: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol, directly counteract the effects of phenylephrine and can counter the desired pharmacologic effect. They also can be used to treat excessive phenylephrine-induced hypertension.
Acetaminophen; Codeine: (Moderate) Concomitant use of codeine with haloperidol may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. It is recommended to avoid this combination when codeine is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of haloperidol could decrease codeine plasma concentrations and increase morphine plasma concentrations resulting in prolonged opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. If haloperidol is discontinued, monitor the patient carefully and consider reducing the opioid dosage if appropriate. Codeine is primarily metabolized by CYP2D6 to morphine, and by CYP3A4 to norcodeine; norcodeine does not have analgesic properties. Haloperidol is a moderate inhibitor of CYP2D6.
Acetaminophen; Dextromethorphan; Doxylamine: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur.
Acetaminophen; Dextromethorphan; Guaifenesin; Phenylephrine: (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol, directly counteract the effects of phenylephrine and can counter the desired pharmacologic effect. They also can be used to treat excessive phenylephrine-induced hypertension.
Acetaminophen; Dextromethorphan; Phenylephrine: (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol, directly counteract the effects of phenylephrine and can counter the desired pharmacologic effect. They also can be used to treat excessive phenylephrine-induced hypertension.
Acetaminophen; Dextromethorphan; Pseudoephedrine: (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol

directly counteract the effects of pseudoephedrine and can counter the desired pharmacologic effect. They also can be used to treat excessive pseudoephedrine-induced hypertension.
Acetaminophen; Diphenhydramine: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as diphenhydamine, a sedating H1-blocker. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur.
Acetaminophen; Guaifenesin; Phenylephrine: (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol, directly counteract the effects of phenylephrine and can counter the desired pharmacologic effect. They also can be used to treat excessive phenylephrine-induced hypertension.
Acetaminophen; Hydrocodone: (Moderate) Concomitant use of hydrocodone with haloperidol may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of haloperidol could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If haloperidol is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Haloperidol is a moderate inhibitor of CYP2D6.
Acetaminophen; Oxycodone: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as opiate agonists. Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.
Acetaminophen; Pentazocine: (Moderate) Concomitant use of pentazocine with other CNS depressants can potentiate respiratory depression, CNS depression, and sedation. Pentazocine should be used cautiously in any patient receiving these agents, which may include haloperidol.
Acetaminophen; Propoxyphene: (Moderate) Propoxyphene is a substrate and an inhibitor of CYP2D6. Increased serum concentrations of propoxyphene would be expected from concurrent use of a CYP2D6 inhibitor, such as haloperidol.
Acetaminophen; Pseudoephedrine: (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol directly counteract the effects of pseudoephedrine and can counter the desired pharmacologic effect. They also can be used to treat excessive pseudoephedrine-induced hypertension.
Acetaminophen; Tramadol: (Major) Haloperidol can competitively inhibit the metabolism of tramadol by CYP2D6. Concurrent use of haloperidol and tramadol increases plasma levels of tramadol and decreases the concentration of the active tramadol metabolite. This may lead to decreased analgesic effects of tramadol and possibly increased tramadol-induced side effects, including seizures, due to increased tramadol concentrations and the decrease in seizure threshold caused by haloperidol. Additive CNS depression may also be seen with the concomitant use of tramadol and haloperidol.
Acetazolamide: (Major) QT prolongation has been observed during haloperidol treatment. Use of haloperidol and medications known to cause electrolyte imbalance may increase the risk of QT prolongation. Therefore, caution is advisable during concurrent use of haloperidol and acetazolamide.
Acrivastine; Pseudoephedrine: (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol directly counteract the effects of pseudoephedrine and can counter the desired pharmacologic effect. They also can be used to treat excessive pseudoephedrine-induced hypertension.
Aldesleukin, IL-2: (Moderate) Aldesleukin, IL-2 may affect CNS function significantly. Therefore, psychotropic pharmacodynamic interactions could occur following concomitant administration of drugs with significant CNS or psyhcotropic activity. Use with caution.
Alfentanil: (Minor) Haloperidol can potentiate the actions of other CNS depressants, such as opiate agonists, Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.
Alfuzosin: (Major) QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval, including alfuzosin.
Aliskiren; Amlodipine: (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Aliskiren; Amlodipine; Hydrochlorothiazide, HCTZ: (Major) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. The risk of QT prolongation may also be increased during use of haloperidol and medications known to cause electrolyte imbalance such as thiazide diuretics. (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Aliskiren; Hydrochlorothiazide, HCTZ: (Major) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. The risk of QT prolongation may also be increased during use of haloperidol and medications known to cause electrolyte imbalance such as thiazide diuretics.
Aliskiren; Valsartan: (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Alprazolam: (Moderate) Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and CYP3A4 substrates such as alprazolam. Until more data are available, it is advisable to closely monitor for adverse events when alprazolam is coadministered with haloperidol. Concomitant administration of alprazolam with CNS-depressant drugs including antipsychotics can potentiate the CNS effects (e.g., increased sedation or respiratory depression) of either agent.
Amiloride: (Moderate) In general, haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Amiloride; Hydrochlorothiazide, HCTZ: (Major) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. The risk of QT prolongation may also be increased during use of haloperidol and medications known to cause electrolyte imbalance such as thiazide diuretics. (Moderate) In general, haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Amiodarone: (Major) QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval. In addition, haloperidol is a substrate for CYP3A4 and CYP2D6. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and inhibitors of CYP3A4 or CYP2D6. Therefore, it is advisable to closely monitor for adverse events when haloperidol is co-administered with drugs that inhibit CYP3A4 and CYP2D6 and prolong the QT interval, such as amiodarone. Amiodarone, a Class III antiarrhythmic agent, is associated with a well-established risk of QT prolongation and torsades de pointes (TdP). Although the frequency of TdP is less with amiodarone than with other Class III agents, amiodarone is still associated with a risk of TdP. Due to the extremely long half-life of amiodarone, a drug interaction is possible for days to weeks after discontinuation of amiodarone.
Amitriptyline; Chlordiazepoxide: (Moderate) Haloperidol can potentiate the actions of other CNS depressants, such as benzodiazepines, Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.
Amlodipine: (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Amlodipine; Atorvastatin: (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Amlodipine; Benazepril: (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Amlodipine; Hydrochlorothiazide, HCTZ; Olmesartan: (Major) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. The risk of QT prolongation may also be increased during use of haloperidol and medications known to cause electrolyte imbalance such as thiazide diuretics. (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Amlodipine; Hydrochlorothiazide, HCTZ; Valsartan: (Major) In general, antipsychotics like haloperidol should be used cautiously with

antihypertensive agents due to the possibility of additive hypotension. The risk of QT prolongation may also be increased during use of haloperidol and medications known to cause electrolyte imbalance such as thiazide diuretics. (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.

Amlodipine; Olmesartan: (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.

Amlodipine; Telmisartan: (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.

Amlodipine; Valsartan: (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.

Amobarbital: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as barbiturates. Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.

Amoxapine: (Moderate) Use caution during co-administration of amoxapine and antipsychotics. Amoxapine exhibits some antipsychotic activity and may increase the risk of tardive dyskinesia or neuroleptic malignant syndrome (NMS) when antipsychotics are given concurrently. Clinically significant anticholinergic activity may also be seen with loxapine, olanzapine, and clozapine. In addition, amoxapine is metabolized by CYP2D6. Haloperidol is an inhibitor of hepatic CYP2D6, and coadministration with amoxapine may lead to elevated amoxapine serum concentrations.

Amoxicillin; Clarithromycin; Lansoprazole: (Major) Concurrent use of clarithromycin and haloperidol should be avoided if possible. QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval. Because clarithromycin is also associated with an increased risk for QT prolongation and TdP, the need to coadminister clarithromycin with drugs known to prolong the QT interval should be done with a careful assessment of risks versus benefits. Clarithromycin is an inhibitor of CYP3A4. Elevated haloperidol concentrations occurring through inhibition of CYP3A4 or CYP2D6 may increase the risk of adverse effects, including QT prolongation.

Amoxicillin; Clarithromycin; Omeprazole: (Major) Concurrent use of clarithromycin and haloperidol should be avoided if possible. QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval. Because clarithromycin is also associated with an increased risk for QT prolongation and TdP, the need to coadminister clarithromycin with drugs known to prolong the QT interval should be done with a careful assessment of risks versus benefits. Clarithromycin is an inhibitor of CYP3A4. Elevated haloperidol concentrations occurring through inhibition of CYP3A4 or CYP2D6 may increase the risk of adverse effects, including QT prolongation.

Amphetamines: (Major) Concurrent use of antipsychotics and amphetamines should generally be avoided. Antipsychotics and amphetamines may interact pharmacodynamically to diminish the therapeutic effects of either agent through opposing effects on dopamine. Amphetamines are thought to block central dopamine reuptake, which has the potential to exacerbate psychosis, and antipsychotics, which are central dopamine antagonists, may diminish the effectiveness of amphetamines.

Amprenavir: (Moderate) Amprenavir is a CYP3A4 substrate as well as an inhibitor of this isoenzyme. CYP3A4 is one of the isoenzymes responsible for the metabolism of haloperidol. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and substrates or inhibitors of CYP3A4. Elevated haloperidol concentrations occurring through inhibition of CYP3A4 may increase the risk of adverse effects, including QT prolongation. Until more data are available, it is advisable to closely monitor for adverse events when these medications are co-administered. A similar interaction is expected to occur between haloperidol and fosamprenavir, the prodrug of amprenavir.

Anagrelide: (Major) Torsades de pointes (TdP) and ventricular tachycardia have been reported during post-marketing use of anagrelide. A cardiovascular examination, including an ECG, should be obtained in all patients prior to initiating anagrelide therapy. Monitor patients during anagrelide therapy for cardiovascular effects and evaluate as necessary. Drugs with a possible risk for QT prolongation and TdP that should be used cautiously and with close monitoring with anagrelide include haloperidol.

Angiotensin II receptor antagonists: (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.

Angiotensin-converting enzyme inhibitors: (Moderate) In general, haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.

Anthracyclines: (Major) Haloperidol is an inhibitor of CYP2D6 and doxorubicin is a major CYP2D6 substrate. Clinically significant interactions have been reported when doxorubicin was coadministered with inhibitors of CYP2D6, resulting in increased concentration and clinical effect of doxorubicin. Additionally, acute cardiotoxicity can occur during the administration of doxorubicin; although, the incidence is rare. Acute ECG changes during anthracycline therapy are usually transient and include ST-T wave changes, QT prolongation, and changes in QRS voltage. Sinus tachycardia is the most common arrhythmia, but other arrhythmias such as supraventricular tachycardia (SVT), ventricular tachycardia, heart block, and premature ventricular contractions (PVCs) have been reported. Haloperidol has a possible risk of causing QT prolongation and torsades de pointes (TdP). Avoid coadministration of haloperidol and doxorubicin if possible. If not possible, closely monitor for increased side effects of doxorubicin including myelosuppression and cardiotoxicity

Anxiolytics; Sedatives; and Hypnotics: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as anxiolytics, sedatives, and hypnotics, and they should be used cautiously in combination.

Apalutamide: (Moderate) Monitor for decreased efficacy of haloperidol if coadministration with apalutamide is necessary. Haloperidol is a CYP3A4 substrate and apalutamide is a strong CYP3A4 inducer. Coadministration with another strong CYP3A4 inducer decreased haloperidol plasma concentrations by a mean of 70% and increased mean scores on the Brief Psychiatric Rating Scale from baseline.

Apomorphine: (Major) Antipsychotics (neuroleptics) may block the dopamine agonist properties of apomorphine, thereby compromising apomorphine effectiveness. Apomorphine causes considerable somnolence, and concomitant administration of apomorphine and CNS depressants like the antipsychotics could result in additive CNS effects. Limited data indicate that QT prolongation is possible with apomorphine administration; the change in QTc interval is not significant in most patients receiving dosages within the manufacturer's guidelines; however, large increases (> 60 msecs from pre-dose) have occurred. Doses <= 6 mg SC are associated with minimal increases in QTc; doses > 6 mg SC do not provide additional clinical benefit and are not recommended. Apomorphine should be used with caution in patients receiving antipsychotics associated with QT prolongation such as haloperidol. Careful monitoring is recommended during combined use of antipsychotics and apomorphine; dosage adjustments of one or both drugs may be warranted.

Aprepitant, Fosaprepitant: (Major) Use caution if haloperidol and aprepitant, fosaprepitant are used concurrently and monitor for an increase in haloperidol-related adverse effects, including QT prolongation and torsade de pointes (TdP), for several days after administration of a multi-day aprepitant regimen. Haloperidol is a CYP3A4 substrate. Aprepitant, when administered as a 3-day oral regimen (125 mg/80 mg/80 mg), is a moderate CYP3A4 inhibitor and inducer and may increase plasma concentrations of haloperidol. For example, a 5-day oral aprepitant regimen increased the AUC of another CYP3A4 substrate, midazolam (single dose), by 2.3-fold on day 1 and by 3.3-fold on day 5. After a 3-day oral aprepitant regimen, the AUC of midazolam (given on days 1, 4, 8, and 15) increased by 25% on day 4, and then decreased by 19% and 4% on days 8 and 15, respectively. As a single 125 mg or 40 mg oral dose, the inhibitory effect of aprepitant on CYP3A4 is weak, with the AUC of midazolam increased by 1.5-fold and 1.2-fold, respectively. After administration, fosaprepitant is rapidly converted to aprepitant and shares many of the same drug interactions. However, as a single 150 mg intravenous dose, fosaprepitant only weakly inhibits CYP3A4 for a duration of 2 days; there is no evidence of CYP3A4 induction. Fosaprepitant 150 mg IV as a single dose increased the AUC of midazolam (given on days 1 and 4) by approximately 1.8-fold on day 1; there was no effect on day 4. Less than a 2-fold increase in the midazolam AUC is not considered clinically important.

Aripiprazole: (Major) Because both haloperidol and aripiprazole are associated with a possible risk for QT prolongation and torsade de pointes

(TdP), the combination should be used cautiously and with close monitoring. In addition, haloperidol is an inhibitor of CYP2D6 and aripiprazole is a partial substrate for aripiprazole. If these agents are used in combination, the patient should be carefully monitored for aripiprazole-related adverse reactions. Because aripiprazole is also metabolized by CYP3A4, patients receiving a combination of a CYP3A4 and CYP2D6 inhibitor should have their oral aripiprazole dose reduced to one-quarter (25%) of the usual dose with subsequent adjustments based upon clinical response. Adults receiving a combination of a CYP3A4 and CYP2D6 inhibitor for more than 14 days should have their Abilify Maintena dose reduced from 400 mg/month to 200 mg/month or from 300 mg/month to 160 mg/month, respectively. There are no dosing recommendations for Aristada or Aristada Initio during use of a mild to moderate CYP2D6 inhibitor. The risk of drowsiness, dizziness, hypotension, extrapyramidal symptoms, anticholinergic effects, neuroleptic malignant syndrome, or seizures may be increased during combined use; therefore, it may be advisable to initiate treatment with lower dosages if combination therapy is necessary. Although the incidence of tardive dyskinesia from combination antipsychotic therapy has not been established and data are very limited, the risk appears to be increased during use of a conventional and atypical antipsychotic versus use of a conventional antipsychotic alone.

Arsenic Trioxide: (Major) If possible, drugs that are known to prolong the QT interval should be discontinued prior to initiating arsenic trioxide therapy. QT prolongation should be expected with the administration of arsenic trioxide. Torsade de pointes (TdP) and complete atrioventricular block have been reported. Drugs with a possible risk for QT prolongation and TdP that should be used cautiously with arsenic trioxide include haloperidol.

Artemether; Lumefantrine: (Major) Artemether; lumefantrine is an inhibitor of and haloperidol is partially metabolized by the CYP2D6 isoenzyme; therefore, coadministration may lead to increased haloperidol concentrations. Furthermore, although there are no studies examining the effects of artemether; lumefantrine in patients receiving other QT prolonging drugs, coadministration of such drugs may result in additive QT prolongation. Concomitant use of artemether; lumefantrine with drugs that may prolong the QT interval, such as haloperidol, should be avoided. Consider ECG monitoring if haloperidol must be used with or after artemether; lumefantrine treatment.

Articaine; Epinephrine: (Major) Use of epinephrine to treat droperidol or haloperidol -induced hypotension can result in a paradoxical lowering of blood pressure due to droperidol's alpha-blocking effects. Avoid using epinephrine concurrently with droperidol and haloperidol.

Asenapine: (Major) Asenapine has been associated with QT prolongation. According to the manufacturer, asenapine should not be used with other agents also known to have this effect (e.g., haloperidol).

Aspirin, ASA; Butalbital; Caffeine: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as barbiturates. Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.

Aspirin, ASA; Butalbital; Caffeine; Codeine: (Moderate) Concomitant use of codeine with haloperidol may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. It is recommended to avoid this combination when codeine is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of haloperidol could decrease codeine plasma concentrations and increase morphine plasma concentrations resulting in prolonged opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. If haloperidol is discontinued, monitor the patient carefully and consider reducing the opioid dosage if appropriate. Codeine is primarily metabolized by CYP2D6 to morphine, and by CYP3A4 to norcodeine; norcodeine does not have analgesic properties. Haloperidol is a moderate inhibitor of CYP2D6. (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as barbiturates. Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.

Aspirin, ASA; Caffeine; Dihydrocodeine: (Moderate) Concomitant use of a potent CYP2D6 inhibitor like haloperidol with dihydrocodeine-containing products may decrease the metabolism of dihydrocodeine to dihydromorphine. Although theoretical, patients may experience varying degrees of analgesia if they take dihydrocodeine with a CYP2D6 inhibitor.

Aspirin, ASA; Carisoprodol; Codeine: (Moderate) Concomitant use of codeine with haloperidol may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. It is recommended to avoid this combination when codeine is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of haloperidol could decrease codeine plasma concentrations and increase morphine plasma concentrations resulting in prolonged opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. If haloperidol is discontinued, monitor the patient carefully and consider reducing the opioid dosage if appropriate. Codeine is primarily metabolized by CYP2D6 to morphine, and by CYP3A4 to norcodeine; norcodeine does not have analgesic properties. Haloperidol is a moderate inhibitor of CYP2D6.

Aspirin, ASA; Oxycodone: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as opiate agonists. Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.

Atazanavir: (Moderate) Caution should be used in patients receiving atazanavir concurrently with drugs metabolized via CYP3A4 and known to cause QT prolongation. Atazanavir inhibits the CYP3A4 isoenzyme at clinically relevant concentrations, which may lead to increased serum concentrations of the listed drugs and an increased potential for QT prolongation or other adverse effects. Serious and/or life-threatening drug interactions could potentially occur between atazanavir and these drugs. Haloperidol is metabolized by CYP3A4 and with the potential to cause QT prolongation. Avoid use of atazanavir with haloperidol when possible. Downward dosage adjustment of haloperidol may be necessary.

Atazanavir; Cobicistat: (Moderate) Caution is warranted when cobicistat is administered with haloperidol as there is a potential for elevated haloperidol and cobicistat concentrations. Haloperidol is a CYP3A4 substrate and CYP2D6 substrate/inhibitor. Cobicistat is an inhibitor of CYP3A4 and a substrate/inhibitor of CYP2D6. (Moderate) Caution should be used in patients receiving atazanavir concurrently with drugs metabolized via CYP3A4 and known to cause QT prolongation. Atazanavir inhibits the CYP3A4 isoenzyme at clinically relevant concentrations, which may lead to increased serum concentrations of the listed drugs and an increased potential for QT prolongation or other adverse effects. Serious and/or life-threatening drug interactions could potentially occur between atazanavir and these drugs. Haloperidol is metabolized by CYP3A4 and with the potential to cause QT prolongation. Avoid use of atazanavir with haloperidol when possible. Downward dosage adjustment of haloperidol may be necessary.

Atenolol: (Moderate) Haloperidol should be used cautiously with atenolol due to the possibility of additive hypotension.

Atenolol; Chlorthalidone: (Major) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. The risk of QT prolongation may also be increased during use of haloperidol and medications known to cause electrolyte imbalance such as thiazide diuretics. (Moderate) Haloperidol should be used cautiously with atenolol due to the possibility of additive hypotension.

Atomoxetine: (Major) QT prolongation has occurred during therapeutic use of atomoxetine and following overdose. Atomoxetine is considered a drug with a possible risk of torsade de pointes (TdP). Drugs with a possible risk for QT prolongation and TdP that should be used cautiously and with close monitoring with atomoxetine include haloperidol.

Atropine; Benzoic Acid; Hyoscyamine; Methenamine; Methylene Blue; Phenyl Salicylate: (Moderate) Additive adverse effects resulting from cholinergic blockade may occur when hyoscyamine is administered concomitantly with haloperidol.

Atropine; Difenoxin: (Moderate) Haloperidol can potentiate the actions of other CNS depressants, such as opiate agonists, Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.

Atropine; Diphenoxylate: (Moderate) Haloperidol can potentiate the actions of other CNS depressants, such as opiate agonists, Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.

Atropine; Hyoscyamine; Phenobarbital; Scopolamine: (Moderate) Additive adverse effects resulting from cholinergic blockade may occur when hyoscyamine is administered concomitantly with haloperidol. (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as barbiturates. Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.

Azilsartan: (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.

Azilsartan; Chlorthalidone: (Major) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. The risk of QT prolongation may also be increased during use of haloperidol and medications known to cause electrolyte imbalance such as thiazide diuretics. (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.

Azithromycin: (Major) Due to an increased risk for QT prolongation and torsade de pointes (TdP), cautious use of haloperidol with azithromycin is

advised. Azithromycin has been associated with post-marketing reports of QT prolongation and TdP. QT prolongation and TdP have also been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation.
Barbiturates: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as barbiturates. Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.
Bedaquiline: (Major) Due to the potential for QT prolongation and torsade de pointes (TdP), caution is advised when administering bedaquiline with haloperidol. Bedaquiline has been reported to prolong the QT interval. Prior to initiating bedaquiline, obtain serum electrolyte concentrations and a baseline ECG. An ECG should also be performed at least 2, 12, and 24 weeks after starting bedaquiline therapy. QT prolongation and TdP have also been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation.
Belladonna Alkaloids; Ergotamine; Phenobarbital: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as barbiturates. Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.
Belladonna; Opium: (Moderate) Haloperidol can potentiate the actions of other CNS depressants, such as opiate agonists, Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.
Benazepril; Hydrochlorothiazide, HCTZ: (Major) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. The risk of QT prolongation may also be increased during use of haloperidol and medications known to cause electrolyte imbalance such as thiazide diuretics.
Bendroflumethiazide; Nadolol: (Major) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. The risk of QT prolongation may also be increased during use of haloperidol and medications known to cause electrolyte imbalance such as thiazide diuretics. (Moderate) Haloperidol should be used cautiously with nadolol due to the possibility of additive hypotension.
Benzoic Acid; Hyoscyamine; Methenamine; Methylene Blue; Phenyl Salicylate: (Moderate) Additive adverse effects resulting from cholinergic blockade may occur when hyoscyamine is administered concomitantly with haloperidol.
Benztropine: (Moderate) Advise patients to promptly report gastrointestinal complaints, fever, or heat intolerance when benztropine is used with drugs with either anticholinergic activity or antidopaminergic activity (example is haloperidol). Clinicians should note that anticholinergic effects might be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness may also occur.
Bepridil: (Severe) Bepridil administration is associated with a well-established risk of QT prolongation and torsade de pointes (TdP). Patients receiving other drugs which have the potential for QT prolongation, such as haloperidol, have an increased risk of developing proarrhythmias during bepridil therapy. According to the manufacturer, bepridil is contraindicated for use with drugs that prolong the QT interval due to the risk of TdP.
Betaxolol: (Moderate) Haloperidol should be used cautiously with betaxolol due to the possibility of additive hypotension.
Bismuth Subcitrate Potassium; Metronidazole; Tetracycline: (Major) Potential QT prolongation has been reported in limited case reports with metronidazole. Drugs with a possible risk for QT prolongation and TdP that should be used cautiously and with close monitoring with metronidazole include haloperidol.
Bismuth Subsalicylate; Metronidazole; Tetracycline: (Major) Potential QT prolongation has been reported in limited case reports with metronidazole. Drugs with a possible risk for QT prolongation and TdP that should be used cautiously and with close monitoring with metronidazole include haloperidol.
Bisoprolol: (Moderate) Haloperidol should be used cautiously with bisoprolol due to the possibility of additive hypotension.
Bisoprolol; Hydrochlorothiazide, HCTZ: (Major) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. The risk of QT prolongation may also be increased during use of haloperidol and medications known to cause electrolyte imbalance such as thiazide diuretics. (Moderate) Haloperidol should be used cautiously with bisoprolol due to the possibility of additive hypotension.
Boceprevir: (Moderate) Boceprevir is a substrate and inhibitor of CYP3A4, one of the isoenzymes responsible for the metabolism of haloperidol. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and substrates or inhibitors of CYP3A4. Elevated haloperidol concentrations occurring through inhibition of CYP3A4 may increase the risk of adverse effects, including QT prolongation. Until more data are available, it is advisable to closely monitor for adverse events when these medications are co-administered.
Brexpiprazole: (Major) Caution is advisable during concurrent use of brexpiprazole with other antipsychotics such as haloperidol. Brexpiprazole is partially metabolized by CYP2D6 and haloperidol is a moderate inhibitor of CYP2D6. The manufacturer of brexpiprazole recommends that the brexpiprazole dose be reduced to one-quarter (25%) of the usual dose in patients receiving a moderate to strong inhibitor of CYP3A4 in combination with a moderate to strong inhibitor of CYP2D6. Therefore, if haloperidol is used in combination with brexpiprazole and a moderate to strong CYP3A4 inhibitor, the brexpiprazole dose should be adjusted and the patient should be carefully monitored for brexpiprazole-related adverse reactions. The risk of drowsiness, dizziness, hypotension, extrapyramidal symptoms, anticholinergic effects, neuroleptic malignant syndrome, or seizures may be increased during combined use of haloperidol and brexpiprazole; therefore, it may be advisable to initiate treatment with lower dosages if combination therapy is deemed necessary. Although the incidence of tardive dyskinesia from combination antipsychotic therapy has not been established and data are very limited, the risk appears to be increased during use of a conventional and atypical antipsychotic versus use of a conventional antipsychotic alone.
Brigatinib: (Moderate) Monitor for decreased efficacy of haloperidol if coadministration with brigatinib is necessary. Haloperidol is a CYP3A substrate and brigatinib induces CYP3A in vitro; plasma concentrations of haloperidol may decrease. Coadministration with a strong CYP3A4 inducer decreased plasma concentrations of haloperidol by a mean of 70% (n = 12); in 5 other patients, discontinuation of the same strong CYP3A4 inducer increased mean haloperidol concentrations by 3.3-fold.
Brimonidine; Timolol: (Moderate) Haloperidol should be used cautiously with timolol due to the possibility of additive hypotension.
Bromocriptine: (Major) Avoid concurrent use of haloperidol and bromocriptine when possible. Haloperidol results in a decreased efficacy of bromocriptine. The prolactin-lowering effect of bromocriptine is antagonized; the elevation in prolactin levels produced by haloperidol persists with chronic administration. Until more data are available, it is advisable to closely monitor for adverse events when these medications must be co-administered.
Brompheniramine: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur.
Brompheniramine; Carbetapentane; Phenylephrine: (Moderate) Drowsiness has been reported during administration of carbetapentane. An enhanced CNS depressant effect may occur when carbetapentane is combined with other CNS depressants including haloperidol or droperidol. (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol, directly counteract the effects of phenylephrine and can counter the desired pharmacologic effect. They also can be used to treat excessive phenylephrine-induced hypertension.
Brompheniramine; Dextromethorphan; Guaifenesin: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur.
Brompheniramine; Guaifenesin; Hydrocodone: (Moderate) Concomitant use of hydrocodone with haloperidol may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of haloperidol could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If haloperidol is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Haloperidol is a moderate inhibitor of CYP2D6. (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects

may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur.
Brompheniramine; Hydrocodone; Pseudoephedrine: (Moderate) Concomitant use of hydrocodone with haloperidol may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of haloperidol could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If haloperidol is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Haloperidol is a moderate inhibitor of CYP2D6. (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol directly counteract the effects of pseudoephedrine and can counter the desired pharmacologic effect. They also can be used to treat excessive pseudoephedrine-induced hypertension.
Brompheniramine; Pseudoephedrine: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol directly counteract the effects of pseudoephedrine and can counter the desired pharmacologic effect. They also can be used to treat excessive pseudoephedrine-induced hypertension.
Bumetanide: (Major) QT prolongation has been observed during haloperidol treatment. Use of haloperidol and medications known to cause electrolyte imbalance may increase the risk of QT prolongation. Therefore, caution is advisable during concurrent use of haloperidol and loop diuretics. In general, haloperidol should also be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Buprenorphine: (Major) Due to the potential for QT prolongation and additive CNS depressant effects, cautious use and close monitoring are advisable if concurrent use of haloperidol and buprenorphine is necessary. Buprenorphine has been associated with QT prolongation and has a possible risk of torsade de pointes (TdP). Haloperidol has a possible risk for QT prolongation and TdP. FDA-approved labeling for some buprenorphine products recommend avoiding use with Class 1A and Class III antiarrhythmic medications while other labels recommend avoiding use with any drug that has the potential to prolong the QT interval. If concurrent use of haloperidol and buprenorphine is necessary, consider a dose reduction of one or both drugs. Hypotension, profound sedation, coma, respiratory depression, or death may occur during co-administration of buprenorphine and other CNS depressants. Prior to concurrent use of buprenorphine in patients taking a CNS depressant, assess the level of tolerance to CNS depression that has developed, the duration of use, and the patient's overall response to treatment. Evaluate the patient's use of alcohol or illicit drugs. It is recommended that the injectable buprenorphine dose be halved for patients who receive other drugs with CNS depressant effects; for the buprenorphine transdermal patch, start with the 5 mcg/hour patch. Monitor patients for sedation or respiratory depression.
Buprenorphine; Naloxone: (Major) Due to the potential for QT prolongation and additive CNS depressant effects, cautious use and close monitoring are advisable if concurrent use of haloperidol and buprenorphine is necessary. Buprenorphine has been associated with QT prolongation and has a possible risk of torsade de pointes (TdP). Haloperidol has a possible risk for QT prolongation and TdP. FDA-approved labeling for some buprenorphine products recommend avoiding use with Class 1A and Class III antiarrhythmic medications while other labels recommend avoiding use with any drug that has the potential to prolong the QT interval. If concurrent use of haloperidol and buprenorphine is necessary, consider a dose reduction of one or both drugs. Hypotension, profound sedation, coma, respiratory depression, or death may occur during co-administration of buprenorphine and other CNS depressants. Prior to concurrent use of buprenorphine in patients taking a CNS depressant, assess the level of tolerance to CNS depression that has developed, the duration of use, and the patient's overall response to treatment. Evaluate the patient's use of alcohol or illicit drugs. It is recommended that the injectable buprenorphine dose be halved for patients who receive other drugs with CNS depressant effects; for the buprenorphine transdermal patch, start with the 5 mcg/hour patch. Monitor patients for sedation or respiratory depression.
Bupropion: (Major) Bupropion is associated with a dose-related risk of seizures. Extreme caution is recommended during concurrent use of other drugs that may lower the seizure threshold such as antipsychotics. The manufacturer of bupropion recommends low initial dosing and slow dosage titration if this combination must be used; the patient should be closely monitored. In addition, bupropion and hydroxybupropion, the major active metabolite, are inhibitors of CYP2D6 in vitro. Coadministration of bupropion with medications that are metabolized by the CYP2D6 isoenzyme, such as haloperidol, should be approached with caution. Dosage reductions of haloperidol may be needed. Conversely, if bupropion therapy is discontinued, the antipsychotic dosage may need to be increased in some patients.
Bupropion; Naltrexone: (Major) Bupropion is associated with a dose-related risk of seizures. Extreme caution is recommended during concurrent use of other drugs that may lower the seizure threshold such as antipsychotics. The manufacturer of bupropion recommends low initial dosing and slow dosage titration if this combination must be used; the patient should be closely monitored. In addition, bupropion and hydroxybupropion, the major active metabolite, are inhibitors of CYP2D6 in vitro. Coadministration of bupropion with medications that are metabolized by the CYP2D6 isoenzyme, such as haloperidol, should be approached with caution. Dosage reductions of haloperidol may be needed. Conversely, if bupropion therapy is discontinued, the antipsychotic dosage may need to be increased in some patients.
Buspirone: (Moderate) The combination of buspirone and CNS depressants like the antipsychotics can increase the risk for sedation. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and CYP3A4 substrates such as buspirone. Elevated haloperidol concentrations may increase the risk of adverse effects, including QT prolongation. Until more data are available, it is advisable to closely monitor for adverse events when buspirone is coadministered with haloperidol.
Butabarbital: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as barbiturates. Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.
Butorphanol: (Moderate) Concomitant use of butorphanol with other CNS depressants can potentiate the effects of butorphanol on respiratory depression, CNS depression, and sedation. If a CNS depressant needs to be used with butorphanol, use the smallest effective dose and the longest dosing frequency of butorphanol.
Cabergoline: (Major) The prolactin-lowering effect of cabergoline may be antagonized by medications that increase prolactin levels such as the antipsychotic drugs. In addition, cabergoline, which is a dopamine agonist, may diminish the effectiveness of dopamine antagonists such as the antipsychotics.
Candesartan: (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Candesartan; Hydrochlorothiazide, HCTZ: (Major) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. The risk of QT prolongation may also be increased during use of haloperidol and medications known to cause electrolyte imbalance such as thiazide diuretics. (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Captopril; Hydrochlorothiazide, HCTZ: (Major) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. The risk of QT prolongation may also be increased during use of haloperidol and medications known to cause electrolyte imbalance such as thiazide diuretics.
Carbamazepine: (Major) Carbamazepine may potentially accelerate the hepatic metabolism of haloperidol. Dosage adjustments may be necessary, and closer monitoring of clinical and/or adverse effects is warranted when carbamazepine is used with haloperidol.
Carbetapentane; Chlorpheniramine: (Moderate) Drowsiness has been reported during administration of carbetapentane. An enhanced CNS depressant effect may occur when carbetapentane is combined with other CNS depressants including haloperidol or droperidol. (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur.
Carbetapentane; Chlorpheniramine; Phenylephrine: (Moderate) Drowsiness has been reported during administration of carbetapentane. An enhanced CNS depressant effect may occur when carbetapentane is combined with other CNS depressants including haloperidol or droperidol. (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may

occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol, directly counteract the effects of phenylephrine and can counter the desired pharmacologic effect. They also can be used to treat excessive phenylephrine-induced hypertension.

Carbetapentane; Diphenhydramine; Phenylephrine: (Moderate) Drowsiness has been reported during administration of carbetapentane. An enhanced CNS depressant effect may occur when carbetapentane is combined with other CNS depressants including haloperidol or droperidol. (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as diphenhydamine, a sedating H1-blocker. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol, directly counteract the effects of phenylephrine and can counter the desired pharmacologic effect. They also can be used to treat excessive phenylephrine-induced hypertension.

Carbetapentane; Guaifenesin: (Moderate) Drowsiness has been reported during administration of carbetapentane. An enhanced CNS depressant effect may occur when carbetapentane is combined with other CNS depressants including haloperidol or droperidol.

Carbetapentane; Guaifenesin; Phenylephrine: (Moderate) Drowsiness has been reported during administration of carbetapentane. An enhanced CNS depressant effect may occur when carbetapentane is combined with other CNS depressants including haloperidol or droperidol. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol, directly counteract the effects of phenylephrine and can counter the desired pharmacologic effect. They also can be used to treat excessive phenylephrine-induced hypertension.

Carbetapentane; Phenylephrine: (Moderate) Drowsiness has been reported during administration of carbetapentane. An enhanced CNS depressant effect may occur when carbetapentane is combined with other CNS depressants including haloperidol or droperidol. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol, directly counteract the effects of phenylephrine and can counter the desired pharmacologic effect. They also can be used to treat excessive phenylephrine-induced hypertension.

Carbetapentane; Phenylephrine; Pyrilamine: (Moderate) Drowsiness has been reported during administration of carbetapentane. An enhanced CNS depressant effect may occur when carbetapentane is combined with other CNS depressants including haloperidol or droperidol. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol, directly counteract the effects of phenylephrine and can counter the desired pharmacologic effect. They also can be used to treat excessive phenylephrine-induced hypertension.

Carbetapentane; Pseudoephedrine: (Moderate) Drowsiness has been reported during administration of carbetapentane. An enhanced CNS depressant effect may occur when carbetapentane is combined with other CNS depressants including haloperidol or droperidol. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol directly counteract the effects of pseudoephedrine and can counter the desired pharmacologic effect. They also can be used to treat excessive pseudoephedrine-induced hypertension.

Carbetapentane; Pyrilamine: (Moderate) Drowsiness has been reported during administration of carbetapentane. An enhanced CNS depressant effect may occur when carbetapentane is combined with other CNS depressants including haloperidol or droperidol.

Carbidopa; Levodopa: (Major) Antipsychotic agents may inhibit the clinical antiparkinsonian response to levodopa by blocking dopamine receptors in the brain. Haloperidol should be avoided during therapy for Parkinson's disease unless the benefit of the drug outweighs the risk of decreased therapeutic response to levodopa or other treatments.

Carbidopa; Levodopa; Entacapone: (Major) Antipsychotic agents may inhibit the clinical antiparkinsonian response to levodopa by blocking dopamine receptors in the brain. Haloperidol should be avoided during therapy for Parkinson's disease unless the benefit of the drug outweighs the risk of decreased therapeutic response to levodopa or other treatments. (Major) COMT inhibitors should be given cautiously with other agents that cause CNS depression, including haloperidol, due to the possibility of additive sedation.

Carbinoxamine: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur.

Carbinoxamine; Dextromethorphan; Pseudoephedrine: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol directly counteract the effects of pseudoephedrine and can counter the desired pharmacologic effect. They also can be used to treat excessive pseudoephedrine-induced hypertension.

Carbinoxamine; Hydrocodone; Phenylephrine: (Moderate) Concomitant use of hydrocodone with haloperidol may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of haloperidol could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If haloperidol is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Haloperidol is a moderate inhibitor of CYP2D6. (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol, directly counteract the effects of phenylephrine and can counter the desired pharmacologic effect. They also can be used to treat excessive phenylephrine-induced hypertension.

Carbinoxamine; Hydrocodone; Pseudoephedrine: (Moderate) Concomitant use of hydrocodone with haloperidol may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of haloperidol could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If haloperidol is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Haloperidol is a moderate inhibitor of CYP2D6. (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol directly counteract the effects of pseudoephedrine and can counter the desired pharmacologic effect. They also can be used to treat excessive pseudoephedrine-induced hypertension.

Carbinoxamine; Phenylephrine: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol, directly counteract the effects of phenylephrine and can counter the desired pharmacologic effect. They also can be used to treat excessive phenylephrine-induced hypertension.

Carbinoxamine; Pseudoephedrine: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol directly counteract the effects of pseudoephedrine and can counter the desired pharmacologic effect. They also can be used to treat excessive pseudoephedrine-induced hypertension.

Cariprazine: (Major) Avoid use of these drugs together due to duplicative therapeutic effects and additive risks for drowsiness, dizziness, orthostatic hypotension, extrapyramidal symptoms, neuroleptic malignant syndrome, and seizures. Cariprazine, like other antipsychotics, has the potential to impair judgment, thinking, or motor skills. The use of cariprazine with other antipsychotic agents, such as haloperidol, would be expected to have additive risks for pharmacologic effects and adverse reactions. Although the incidence of tardive dyskinesia from combination antipsychotic therapy has not been established and data are very limited, the risk appears to be increased during combined use of a conventional and atypical antipsychotic versus use of a conventional antipsychotic alone.

Carteolol: (Moderate) Haloperidol should be used cautiously with carteolol due to the possibility of additive hypotension.
Carvedilol: (Moderate) Haloperidol should be used cautiously with carvedilol due to the possibility of additive hypotension. In addition, haloperidol inhibits CYP 2D6 and may increase plasma concentrations of carvedilol.
Central-acting adrenergic agents: (Moderate) Disturbances of orthostatic regulation (e.g., orthostatic hypotension, dizziness, fatigue) and additive sedation may occur in patients receiving concomitant clonidine and antipsychotics. Also, based on observations in patients in a state of alcoholic delirium, high intravenous doses of clonidine may increase the arrhythmogenic potential (QT prolongation, ventricular fibrillation) of high intravenous doses of haloperidol. A causal relationship and relevance for clonidine oral tablets have not been established.
Ceritinib: (Major) Periodically monitor electrolytes and ECGs if coadministration with haloperidol is necessary; an interruption of ceritinib therapy, dose reduction, or discontinuation of therapy may be necessary if QT prolongation occurs. Ceritinib causes concentration-dependent prolongation of the QT interval. QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment; excessive doses (particularly in the overdose setting) or IV administration may be associated with a higher risk.
Cetirizine: (Moderate) Additive drowsiness may occur if cetirizine or levocetirizine is administered with other drugs that depress the CNS (e.g., haloperidol).
Cetirizine; Pseudoephedrine: (Moderate) Additive drowsiness may occur if cetirizine or levocetirizine is administered with other drugs that depress the CNS (e.g., haloperidol). (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol directly counteract the effects of pseudoephedrine and can counter the desired pharmacologic effect. They also can be used to treat excessive pseudoephedrine-induced hypertension.
Cetrorelix: (Moderate) Antipsychotics cause hyperprolactinemia and should not be administered concomitantly with cetrorelix since hyperprolactinemia downregulates the number of pituitary GnRH receptors.
Cevimeline: (Moderate) Cevimeline is metabolized by cytochrome P450 3A4 and CYP2D6. Concurrent administration of other agents metabolized through this pathway, such as haloperidol, may lead to increased cevimeline plasma concentrations.
Chlophedianol; Dexchlorpheniramine; Pseudoephedrine: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol directly counteract the effects of pseudoephedrine and can counter the desired pharmacologic effect. They also can be used to treat excessive pseudoephedrine-induced hypertension.
Chlophedianol; Guaifenesin; Phenylephrine: (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol, directly counteract the effects of phenylephrine and can counter the desired pharmacologic effect. They also can be used to treat excessive phenylephrine-induced hypertension.
Chloral Hydrate: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as anxiolytics, sedatives, and hypnotics, and they should be used cautiously in combination.
Chloramphenicol: (Moderate) Chloramphenicol is an inhibitor of CYP3A4, one of the isoenzymes responsible for the metabolism of haloperidol. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and inhibitors of CYP3A4. Until more data are available, it is advisable to closely monitor for adverse events when these medications are co-administered.
Chlorcyclizine: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur.
Chlordiazepoxide: (Moderate) Haloperidol can potentiate the actions of other CNS depressants, such as benzodiazepines, Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.
Chlordiazepoxide; Clidinium: (Moderate) Haloperidol can potentiate the actions of other CNS depressants, such as benzodiazepines, Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.
Chloroquine: (Major) Coadminister chloroquine with other drugs known to prolong the QT interval, such as haloperidol, with caution. Chloroquine is associated with an increased risk of QT prolongation and torsade de pointes (TdP); fatalities have been reported. The risk of QT prolongation is increased with higher chloroquine doses. QT prolongation and TdP have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation.
Chlorothiazide: (Major) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. The risk of QT prolongation may also be increased during use of haloperidol and medications known to cause electrolyte imbalance such as thiazide diuretics.
Chlorpheniramine: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur.
Chlorpheniramine; Codeine: (Moderate) Concomitant use of codeine with haloperidol may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. It is recommended to avoid this combination when codeine is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of haloperidol could decrease codeine plasma concentrations and increase morphine plasma concentrations resulting in prolonged opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. If haloperidol is discontinued, monitor the patient carefully and consider reducing the opioid dosage if appropriate. Codeine is primarily metabolized by CYP2D6 to morphine, and by CYP3A4 to norcodeine; norcodeine does not have analgesic properties. Haloperidol is a moderate inhibitor of CYP2D6. (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur.
Chlorpheniramine; Dextromethorphan: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur.
Chlorpheniramine; Dextromethorphan; Phenylephrine: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol, directly counteract the effects of phenylephrine and can counter the desired pharmacologic effect. They also can be used to treat excessive phenylephrine-induced hypertension.
Chlorpheniramine; Dihydrocodeine; Phenylephrine: (Moderate) Concomitant use of a potent CYP2D6 inhibitor like haloperidol with dihydrocodeine-containing products may decrease the metabolism of dihydrocodeine to dihydromorphine. Although theoretical, patients may experience varying degrees of analgesia if they take dihydrocodeine with a CYP2D6 inhibitor. (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol, directly counteract the effects of phenylephrine and can counter the desired pharmacologic effect. They also can be used to treat excessive phenylephrine-induced hypertension.
Chlorpheniramine; Dihydrocodeine; Pseudoephedrine: (Moderate) Concomitant use of a potent CYP2D6 inhibitor like haloperidol with dihydrocodeine-containing products may decrease the metabolism of dihydrocodeine to dihydromorphine. Although theoretical, patients may experience varying degrees of analgesia if they take dihydrocodeine with a CYP2D6 inhibitor. (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol directly counteract the effects of pseudoephedrine and can counter the desired pharmacologic effect. They also can be used to treat excessive pseudoephedrine-induced hypertension.
Chlorpheniramine; Guaifenesin; Hydrocodone; Pseudoephedrine: (Moderate) Concomitant use of hydrocodone with haloperidol may increase

hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of haloperidol could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If haloperidol is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Haloperidol is a moderate inhibitor of CYP2D6. (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol directly counteract the effects of pseudoephedrine and can counter the desired pharmacologic effect. They also can be used to treat excessive pseudoephedrine-induced hypertension.

Chlorpheniramine; Hydrocodone: (Moderate) Concomitant use of hydrocodone with haloperidol may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of haloperidol could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If haloperidol is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Haloperidol is a moderate inhibitor of CYP2D6. (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur.

Chlorpheniramine; Hydrocodone; Phenylephrine: (Moderate) Concomitant use of hydrocodone with haloperidol may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of haloperidol could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If haloperidol is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Haloperidol is a moderate inhibitor of CYP2D6. (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol, directly counteract the effects of phenylephrine and can counter the desired pharmacologic effect. They also can be used to treat excessive phenylephrine-induced hypertension.

Chlorpheniramine; Hydrocodone; Pseudoephedrine: (Moderate) Concomitant use of hydrocodone with haloperidol may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of haloperidol could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If haloperidol is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Haloperidol is a moderate inhibitor of CYP2D6. (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol directly counteract the effects of pseudoephedrine and can counter the desired pharmacologic effect. They also can be used to treat excessive pseudoephedrine-induced hypertension.

Chlorpheniramine; Phenylephrine: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol, directly counteract the effects of phenylephrine and can counter the desired pharmacologic effect. They also can be used to treat excessive phenylephrine-induced hypertension.

Chlorpheniramine; Pseudoephedrine: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol directly counteract the effects of pseudoephedrine and can counter the desired pharmacologic effect. They also can be used to treat excessive pseudoephedrine-induced hypertension.

Chlorpromazine: (Major) Chlorpromazine, a phenothiazine, is associated with an established risk of QT prolongation and torsade de pointes (TdP). Other antipsychotics associated with a possible risk for QT prolongation and TdP which should be avoided during treatment with chlorpromazine include haloperidol. Coadministration may increase the risk of adverse effects such as drowsiness, dizziness, orthostatic hypotension, anticholinergic effects, extrapyramidal symptoms, neuroleptic malignant syndrome, or seizures. The likelihood of these pharmacodynamic interactions varies based upon the individual properties of the co-administered antipsychotic agent. Although the incidence of tardive dyskinesia from combination antipsychotic therapy has not been established and data are very limited, the risk appears to be increased during use of a conventional and atypical antipsychotic versus use of a conventional antipsychotic alone.

Chlorthalidone: (Major) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. The risk of QT prolongation may also be increased during use of haloperidol and medications known to cause electrolyte imbalance such as thiazide diuretics.

Chlorthalidone; Clonidine: (Major) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. The risk of QT prolongation may also be increased during use of haloperidol and medications known to cause electrolyte imbalance such as thiazide diuretics. (Moderate) Disturbances of orthostatic regulation (e.g., orthostatic hypotension, dizziness, fatigue) and additive sedation may occur in patients receiving concomitant clonidine and antipsychotics. Also, based on observations in patients in a state of alcoholic delirium, high intravenous doses of clonidine may increase the arrhythmogenic potential (QT prolongation, ventricular fibrillation) of high intravenous doses of haloperidol. A causal relationship and relevance for clonidine oral tablets have not been established.

Cinacalcet: (Moderate) Cinacalcet is a substrate of CYP3A4 and an inhibitor of CYP2D6, the isoenzymes responsible for the metabolism of haloperidol. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and substrates or inhibitors of CYP3A4 or CYP2D6. Elevated haloperidol concentrations occurring through inhibition of CYP2D6 or CYP3A4 may increase the risk of adverse effects, including QT prolongation. Until more data are available, it is advisable to closely monitor for adverse events when these medications are co-administered.

Ciprofloxacin: (Major) Due to an increased risk for QT prolongation and torsade de pointes (TdP), caution is advised when administering haloperidol with ciprofloxacin. QT prolongation and TdP have been observed during haloperidol treatment, and ciprofloxacin is associated with a possible risk of QT prolongation and TdP. Excessive haloperidol doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation.

Cisapride: (Severe) Cisapride is associated with QT prolongation and torsade de pointes (TdP) and cisapride is contraindicated for use in patients taking other drugs known to prolong the QT interval. Both QT prolongation and TdP have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. Because of the potential for torsade de pointes (TdP), use of cisapride with haloperidol is contraindicated.

Citalopram: (Major) Coadministration of citalopram and haloperidol should be avoided. Citalopram causes dose-dependent QT interval prolongation, and haloperidol is associated with a possible risk for QT prolongation and torsade de pointes (TdP). If concurrent therapy is

considered essential, ECG monitoring is recommended. In addition, because of the potential risk and severity of serotonin syndrome or neuroleptic malignant syndrome-like reactions, caution should be observed when administering citalopram with drugs that are dopamine antagonists such as haloperidol. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death. Serotonin syndrome, in its most severe form, can resemble neuroleptic malignant syndrome. In addition, citalopram mildly inhibits the CYP2D6. This can result in increased concentrations of some drugs metabolized via the same pathway, including haloperidol. Patients receiving these combinations should be monitored for the emergence of serotonin syndrome, neuroleptic malignant syndrome-like reactions, or other adverse effects.
Clarithromycin: (Major) Concurrent use of clarithromycin and haloperidol should be avoided if possible. QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval. Because clarithromycin is also associated with an increased risk for QT prolongation and TdP, the need to coadminister clarithromycin with drugs known to prolong the QT interval should be done with a careful assessment of risks versus benefits. Clarithromycin is an inhibitor of CYP3A4. Elevated haloperidol concentrations occurring through inhibition of CYP3A4 or CYP2D6 may increase the risk of adverse effects, including QT prolongation.
Clemastine: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur.
Clobazam: (Major) A dosage reduction of CYP2D6 substrates, such as haloperidol, may be necessary during co-administration of clobazam. Limited in vivo data suggest that clobazam is an inhibitor of CYP2D6. Elevated concentrations of haloperidol occurring through inhibition of CYP2D6 may increase the risk of adverse effects, including QT prolongation and torsade de pointes. Clobazam, a benzodiazepine, may cause drowsiness or other CNS effects which may be potentiated during concurrent use of conventional antipsychotics including phenothiazines, haloperidol, loxapine, thiothixene, or molindone. Antipsychotics may lower the seizure threshold and reduce the effectiveness of clobazam as an anticonvulsant.
Clonazepam: (Moderate) Haloperidol can potentiate the actions of other CNS depressants, such as benzodiazepines, Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.
Clonidine: (Moderate) Disturbances of orthostatic regulation (e.g., orthostatic hypotension, dizziness, fatigue) and additive sedation may occur in patients receiving concomitant clonidine and antipsychotics. Also, based on observations in patients in a state of alcoholic delirium, high intravenous doses of clonidine may increase the arrhythmogenic potential (QT prolongation, ventricular fibrillation) of high intravenous doses of haloperidol. A causal relationship and relevance for clonidine oral tablets have not been established.
Clorazepate: (Moderate) Haloperidol can potentiate the actions of other CNS depressants, such as benzodiazepines, Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.
Clozapine: (Major) Treatment with clozapine has been associated with QT prolongation, torsade de pointes (TdP), cardiac arrest, and sudden death. Haloperidol is also associated with a possible risk for QT prolongation and TdP. In addition, coadministration may increase the risk of adverse effects such as drowsiness, dizziness, orthostatic hypotension, anticholinergic effects, extrapyramidal symptoms, neuroleptic malignant syndrome, or seizures. The likelihood of these pharmacodynamic interactions varies based upon the individual properties of the co-administered antipsychotic agent. Although the incidence of tardive dyskinesia from combination antipsychotic therapy has not been established and data are very limited, the risk appears to be increased during use of a conventional and atypical antipsychotic versus use of a conventional antipsychotic alone. Clozapine is metabolized by CYP1A2, CYP3A4, and CYP2D6. Antipsychotic drugs known to inhibit the activity of CYP2D6 include haloperidol. Elevated plasma concentrations of clozapine occurring through inhibition of CYP1A2, CYP3A4, or CYP2D6 may potentially increase the risk of life-threatening arrhythmias, sedation, anticholinergic effects, seizures, orthostasis, or other adverse effects. According to the manufacturer, patients receiving clozapine in combination with an inhibitor of CYP2D6 should be monitored for adverse reactions. Consideration should be given to reducing the clozapine dose if necessary. If the inhibitor is discontinued after dose adjustments are made, monitor for lack of clozapine effectiveness and consider increasing the clozapine dose if necessary.
Cobicistat: (Moderate) Caution is warranted when cobicistat is administered with haloperidol as there is a potential for elevated haloperidol and cobicistat concentrations. Haloperidol is a CYP3A4 substrate and CYP2D6 substrate/inhibitor. Cobicistat is an inhibitor of CYP3A4 and a substrate/inhibitor of CYP2D6.
Cobicistat; Elvitegravir; Emtricitabine; Tenofovir Alafenamide: (Moderate) Caution is warranted when cobicistat is administered with haloperidol as there is a potential for elevated haloperidol and cobicistat concentrations. Haloperidol is a CYP3A4 substrate and CYP2D6 substrate/inhibitor. Cobicistat is an inhibitor of CYP3A4 and a substrate/inhibitor of CYP2D6.
Cobicistat; Elvitegravir; Emtricitabine; Tenofovir Disoproxil Fumarate: (Moderate) Caution is warranted when cobicistat is administered with haloperidol as there is a potential for elevated haloperidol and cobicistat concentrations. Haloperidol is a CYP3A4 substrate and CYP2D6 substrate/inhibitor. Cobicistat is an inhibitor of CYP3A4 and a substrate/inhibitor of CYP2D6.
Codeine: (Moderate) Concomitant use of codeine with haloperidol may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. It is recommended to avoid this combination when codeine is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of haloperidol could decrease codeine plasma concentrations and increase morphine plasma concentrations resulting in prolonged opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. If haloperidol is discontinued, monitor the patient carefully and consider reducing the opioid dosage if appropriate. Codeine is primarily metabolized by CYP2D6 to morphine, and by CYP3A4 to norcodeine; norcodeine does not have analgesic properties. Haloperidol is a moderate inhibitor of CYP2D6.
Codeine; Guaifenesin: (Moderate) Concomitant use of codeine with haloperidol may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. It is recommended to avoid this combination when codeine is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of haloperidol could decrease codeine plasma concentrations and increase morphine plasma concentrations resulting in prolonged opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. If haloperidol is discontinued, monitor the patient carefully and consider reducing the opioid dosage if appropriate. Codeine is primarily metabolized by CYP2D6 to morphine, and by CYP3A4 to norcodeine; norcodeine does not have analgesic properties. Haloperidol is a moderate inhibitor of CYP2D6.
Codeine; Phenylephrine; Promethazine: (Major) Promethazine, a phenothiazine, is associated with a possible risk for QT prolongation. Due to the risk of additive QT prolongation and potential for serious arrhythmias, promethazine should be used with caution in patients receiving haloperidol. In addition, co-administration of promethazine with haloperidol may increase the risk of adverse effects such as drowsiness, dizziness, orthostatic hypotension, anticholinergic effects, extrapyramidal symptoms, neuroleptic malignant syndrome, or seizures. Although the incidence of tardive dyskinesia from these combinations has not been established and data are very limited, the risk may be increased during combined use versus use of an antipsychotic alone. if use together is not avoidable, monitor closely. (Moderate) Concomitant use of codeine with haloperidol may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. It is recommended to avoid this combination when codeine is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of haloperidol could decrease codeine plasma concentrations and increase morphine plasma concentrations resulting in prolonged opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. If haloperidol is discontinued, monitor the patient carefully and consider reducing the opioid dosage if appropriate. Codeine is primarily metabolized by CYP2D6 to morphine, and by CYP3A4 to norcodeine; norcodeine does not have analgesic properties. Haloperidol is a moderate inhibitor of CYP2D6. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol, directly counteract the effects of phenylephrine and can counter the desired pharmacologic effect. They also can be used to treat excessive phenylephrine-induced hypertension.
Codeine; Promethazine: (Major) Promethazine, a phenothiazine, is associated with a possible risk for QT prolongation. Due to the risk of additive QT prolongation and potential for serious arrhythmias, promethazine should be used with caution in patients receiving haloperidol. In addition, co-administration of promethazine with haloperidol may increase the risk of adverse effects such as drowsiness, dizziness, orthostatic hypotension,

anticholinergic effects, extrapyramidal symptoms, neuroleptic malignant syndrome, or seizures. Although the incidence of tardive dyskinesia from these combinations has not been established and data are very limited, the risk may be increased during combined use versus use of an antipsychotic alone. if use together is not avoidable, monitor closely. (Moderate) Concomitant use of codeine with haloperidol may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. It is recommended to avoid this combination when codeine is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of haloperidol could decrease codeine plasma concentrations and increase morphine plasma concentrations resulting in prolonged opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. If haloperidol is discontinued, monitor the patient carefully and consider reducing the opioid dosage if appropriate. Codeine is primarily metabolized by CYP2D6 to morphine, and by CYP3A4 to norcodeine; norcodeine does not have analgesic properties. Haloperidol is a moderate inhibitor of CYP2D6.

COMT inhibitors: (Major) COMT inhibitors should be given cautiously with other agents that cause CNS depression, including haloperidol, due to the possibility of additive sedation.

Conivaptan: (Moderate) Conivaptan is a substrate and inhibitor of CYP3A4, one of the isoenzymes responsible for the metabolism of haloperidol. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and substrates or inhibitors of CYP3A4. Elevated haloperidol concentrations occurring through inhibition of CYP3A4 may increase the risk of adverse effects, including QT prolongation. Until more data are available, it is advisable to closely monitor for adverse events when these medications are co-administered.

Corticosteroids: (Major) QT prolongation has been observed during haloperidol treatment. Use of haloperidol and medications known to cause electrolyte imbalance may increase the risk of QT prolongation. Therefore, caution is advisable during concurrent use of haloperidol and corticosteroids. Topical corticosteroids are less likely to interact.

Crizotinib: (Major) Monitor ECGs for QT prolongation and monitor electrolytes in patients receiving crizotinib concomitantly with haloperidol; an increase in haloperidol exposure may also occur. An interruption of therapy, dose reduction, or discontinuation of therapy may be necessary for crizotinib patients if QT prolongation occurs. Haloperidol is a CYP3A4 substrate that has been associated with QT prolongation and torsade de pointes (TdP); excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. Crizotinib is a moderate CYP3A4 inhibitor that has also been associated with concentration-dependent QT prolongation.

Cyclobenzaprine: (Major) Because both cyclobenzaprine and haloperidol have a possible risk for QT prolongation and torsade de pointes (TdP), this combination should be used together cautiously. Cyclobenzaprine is structurally similar to tricyclic antidepressants, and tricyclic antidepressants have been reported to prolong the QT interval, especially when given in excessive doses (or in overdosage settings).

Cyproheptadine: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur.

Danazol: (Moderate) Danazol is an inhibitor of CYP3A4, one of the isoenzymes responsible for the metabolism of haloperidol. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and inhibitors of CYP3A4. Until more data are available, it is advisable to closely monitor for adverse events when these medications are co-administered.

Dantrolene: (Moderate) Simultaneous use of skeletal muscle relaxants and other CNS depressants, such as antipsychotics, can increase CNS depression.

Darifenacin: (Moderate) Haloperidol inhibits CYP2D6. Serum concentrations of darifenacin, a CYP2D6 substrate, may increase when used in combination with haloperidol. Patients should be monitored for increased anticholinergic side effects if these drugs are coadministered.

Darunavir: (Moderate) Darunavir is a substrate and inhibitor of CYP3A4, one of the isoenzymes responsible for the metabolism of haloperidol. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and substrates or inhibitors of CYP3A4. Until more data are available, it is advisable to closely monitor for adverse events when these medications are co-administered.

Darunavir; Cobicistat: (Moderate) Caution is warranted when cobicistat is administered with haloperidol as there is a potential for elevated haloperidol and cobicistat concentrations. Haloperidol is a CYP3A4 substrate and CYP2D6 substrate/inhibitor. Cobicistat is an inhibitor of CYP3A4 and a substrate/inhibitor of CYP2D6. (Moderate) Darunavir is a substrate and inhibitor of CYP3A4, one of the isoenzymes responsible for the metabolism of haloperidol. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and substrates or inhibitors of CYP3A4. Until more data are available, it is advisable to closely monitor for adverse events when these medications are co-administered.

Darunavir; Cobicistat; Emtricitabine; Tenofovir alafenamide: (Moderate) Caution is warranted when cobicistat is administered with haloperidol as there is a potential for elevated haloperidol and cobicistat concentrations. Haloperidol is a CYP3A4 substrate and CYP2D6 substrate/inhibitor. Cobicistat is an inhibitor of CYP3A4 and a substrate/inhibitor of CYP2D6. (Moderate) Darunavir is a substrate and inhibitor of CYP3A4, one of the isoenzymes responsible for the metabolism of haloperidol. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and substrates or inhibitors of CYP3A4. Until more data are available, it is advisable to closely monitor for adverse events when these medications are co-administered.

Dasabuvir; Ombitasvir; Paritaprevir; Ritonavir: (Major) Ritonavir is an inhibitor of CYP2D6 and CYP3A4, the isoenzymes responsible for the metabolism of haloperidol. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and inhibitors of CYP3A4 or CYP2D6. Elevated haloperidol concentrations occurring through inhibition of CYP2D6 or CYP3A4 may increase the risk of adverse effects, including QT prolongation. In addition, ritonavir also is associated with QT prolongation; concomitant use increases the risk of QT prolongation. Until more data are available, it is advisable to closely monitor for adverse events when these medications are co-administered.

Dasatinib: (Major) Monitor for evidence of QT prolongation and torsade de pointes (TdP) if dasatinib and haloperidol are coadministered. In vitro studies have shown that dasatinib has the potential to prolong the QT interval. QT prolongation and TdP have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation.

Degarelix: (Major) QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval. Drugs with a possible risk for QT prolongation and TdP that should be used cautiously with haloperidol include degarelix.

Delavirdine: (Moderate) Delavirdine is an inhibitor of CYP2D6. Coadministration may result in decreased haloperidol metabolism and increased toxicity with concurrent use. Neurologic side effects have been noted clinically in some patients as a result of impaired haloperidol elimination.

Desflurane: (Major) QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval. Drugs with a possible risk for QT prolongation and TdP that should be used cautiously and with close monitoring with haloperidol include halogenated anesthetics.

Desloratadine; Pseudoephedrine: (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol directly counteract the effects of pseudoephedrine and can counter the desired pharmacologic effect. They also can be used to treat excessive pseudoephedrine-induced hypertension.

Desvenlafaxine: (Major) Although clinical studies have shown that desvenlafaxine does not have a clinically relevant effect on CYP2D6 inhibition at doses of 100 mg/day, the manufacturer recommends that primary substrates of CYP2D6, such as haloperidol, be dosed at the original level when co-administered with desvenlafaxine 100 mg or lower or when desvenlafaxine is discontinued. The dose of these CYP2D6 substrates should be reduced by up to one-half if co-administered with desvenlafaxine 400 mg/day.

Deutetrabenazine: (Major) For patients taking a deutetrabenazine dosage more than 24 mg/day with haloperidol, assess the QTc interval before and after increasing the dosage of either medication. Use caution when prescribing haloperidol concurrently with medications known to prolong the QT interval. Clinically relevant QTc prolongation may occur with deutetrabenazine. QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. Monitor for signs and symptoms of neuroleptic malignant syndrome (NMS), restlessness, and agitation. If NMS is diagnosed, immediately discontinue deutetrabenazine, and provide intensive symptomatic treatment and medical monitoring. Recurrence of NMS

has been reported with resumption of drug therapy. If akathisia or parkinsonism develops during treatment, the deutetrabenazine dose should be reduced; discontinuation may be required. Deutetrabenazine is a reversible, dopamine depleting drug and haloperidol is a dopamine antagonist. Additionally, concurrent use of deutetrabenazine and drugs that can cause CNS depression, such as haloperidol, may have additive effects and worsen drowsiness or sedation. Advise patients about worsened somnolence and not to drive or perform other tasks requiring mental alertness until they know how deutetrabenazine affects them.

Dexchlorpheniramine: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur.

Dexchlorpheniramine; Dextromethorphan; Pseudoephedrine: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol directly counteract the effects of pseudoephedrine and can counter the desired pharmacologic effect. They also can be used to treat excessive pseudoephedrine-induced hypertension.

Dexmethylphenidate: (Moderate) Antipsychotics, such as haloperidol, and dexmethylphenidate may interact pharmacodynamically to diminish the therapeutic effects of either agent through opposing effects on dopamine. Dexmethylphenidate blocks central dopamine reuptake, which has the potential to exacerbate psychosis, and antipsychotics, which are central dopamine antagonists, may diminish the effectiveness of dexmethylphenidate.

Dextromethorphan; Diphenhydramine; Phenylephrine: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as diphenhydamine, a sedating H1-blocker. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol, directly counteract the effects of phenylephrine and can counter the desired pharmacologic effect. They also can be used to treat excessive phenylephrine-induced hypertension.

Dextromethorphan; Guaifenesin; Phenylephrine: (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol, directly counteract the effects of phenylephrine and can counter the desired pharmacologic effect. They also can be used to treat excessive phenylephrine-induced hypertension.

Dextromethorphan; Guaifenesin; Pseudoephedrine: (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol directly counteract the effects of pseudoephedrine and can counter the desired pharmacologic effect. They also can be used to treat excessive pseudoephedrine-induced hypertension.

Dextromethorphan; Promethazine: (Major) Promethazine, a phenothiazine, is associated with a possible risk for QT prolongation. Due to the risk of additive QT prolongation and potential for serious arrhythmias, promethazine should be used with caution in patients receiving haloperidol. In addition, co-administration of promethazine with haloperidol may increase the risk of adverse effects such as drowsiness, dizziness, orthostatic hypotension, anticholinergic effects, extrapyramidal symptoms, neuroleptic malignant syndrome, or seizures. Although the incidence of tardive dyskinesia from these combinations has not been established and data are very limited, the risk may be increased during combined use versus use of an antipsychotic alone. if use together is not avoidable, monitor closely.

Dextromethorphan; Quinidine: (Severe) Quinidine should be considered contraindicated with haloperidol. QT prolongation and torsade de pointes (TdP) have been observed during both haloperidol and quinidine treatment. Excessive doses (particularly in the overdose setting) of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval; however, quinidine is contraindicated for use with drugs that are CYP2D6 substrates that prolong the QT interval. Pretreatment with quinidine caused peak haloperidol serum concentrations and haloperidol AUC to increase.

Diazepam: (Moderate) Haloperidol can potentiate the actions of other CNS depressants, such as benzodiazepines, Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.

Dihydrocodeine; Guaifenesin; Pseudoephedrine: (Moderate) Concomitant use of a potent CYP2D6 inhibitor like haloperidol with dihydrocodeine-containing products may decrease the metabolism of dihydrocodeine to dihydromorphine. Although theoretical, patients may experience varying degrees of analgesia if they take dihydrocodeine with a CYP2D6 inhibitor. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol directly counteract the effects of pseudoephedrine and can counter the desired pharmacologic effect. They also can be used to treat excessive pseudoephedrine-induced hypertension.

Diltiazem: (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. Diltiazem and verapamil are substrates and inhibitors of CYP3A4. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and substrates or inhibitors of CYP3A4 or CYP2D6. Elevated haloperidol concentrations occurring through inhibition of CYP2D6 or CYP3A4 may increase the risk of adverse effects, including QT prolongation.

Dimenhydrinate: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur.

Diphenhydramine: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as diphenhydamine, a sedating H1-blocker. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur.

Diphenhydramine; Hydrocodone; Phenylephrine: (Moderate) Concomitant use of hydrocodone with haloperidol may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of haloperidol could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If haloperidol is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Haloperidol is a moderate inhibitor of CYP2D6. (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as diphenhydamine, a sedating H1-blocker. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol, directly counteract the effects of phenylephrine and can counter the desired pharmacologic effect. They also can be used to treat excessive phenylephrine-induced hypertension.

Diphenhydramine; Ibuprofen: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as diphenhydamine, a sedating H1-blocker. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur.

Diphenhydramine; Naproxen: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as diphenhydamine, a sedating H1-blocker. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur.

Diphenhydramine; Phenylephrine: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as diphenhydamine, a sedating H1-blocker. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol, directly counteract the effects of phenylephrine and can counter the desired pharmacologic effect. They also can be used to treat excessive phenylephrine-induced hypertension.

Disopyramide: (Major) Haloperidol should be used cautiously and with close monitoring with disopyramide. Disopyramide administration is associated with QT prolongation and torsades de pointes (TdP). QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation.

Dofetilide: (Severe) Because of the potential for torsade de pointes (TdP), concurrent use of dofetilide and haloperidol is contraindicated. Dofetilide, a Class III antiarrhythmic agent, is associated with a well-established risk of QT prolongation and TdP. QT prolongation and TdP have been

observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation.
Dolasetron: (Major) Due to a possible risk for QT prolongation and torsade de pointes (TdP), dolasetron and haloperidol should be used together cautiously. Dolasetron has been associated with a dose-dependent prolongation in the QT, PR, and QRS intervals on an electrocardiogram. QT prolongation and TdP have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval.
Dolutegravir; Rilpivirine: (Major) Supratherapeutic doses of rilpivirine (75 to 300 mg/day) have caused QT prolongation; caution is advised when administering rilpivirine with other drugs that may prolong the QT or PR interval, such as haloperidol. QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation.
Donepezil: (Major) Case reports indicate that QT prolongation and torsade de pointes (TdP) can occur during donepezil therapy. Donepezil is considered a drug with a known risk of TdP. Drugs with a possible risk for QT prolongation and TdP that should be used cautiously and with close monitoring with donepezil include haloperidol.
Donepezil; Memantine: (Major) Case reports indicate that QT prolongation and torsade de pointes (TdP) can occur during donepezil therapy. Donepezil is considered a drug with a known risk of TdP. Drugs with a possible risk for QT prolongation and TdP that should be used cautiously and with close monitoring with donepezil include haloperidol.
Dopamine: (Minor) Dopamine infusions intended to improve renal perfusion can be ineffective due to haloperidol's dopamine receptor blockade.
Dorzolamide; Timolol: (Moderate) Haloperidol should be used cautiously with timolol due to the possibility of additive hypotension.
Doxazosin: (Moderate) In general, haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Doxercalciferol: (Moderate) Cytochrome P450 enzyme inhibitors, such as haloperidol, may inhibit the 25-hydroxylation of doxercalciferol, thereby decreasing the formation of the active metabolite and thus, decreasing efficacy.
Doxylamine: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur.
Doxylamine; Pyridoxine: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur.
Dronabinol: (Moderate) Use caution if the use of haloperidol is necessary with dronabinol, and monitor for additive dizziness, confusion, somnolence, and other CNS effects.
Dronedarone: (Severe) The concomitant use of dronedarone and haloperidol is contraindicated. QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. Dronedarone administration is associated with a dose-related increase in the QTc interval. The increase in QTc is approximately 10 milliseconds at doses of 400 mg twice daily (the FDA-approved dose) and up to 25 milliseconds at doses of 1600 mg twice daily. Although there are no studies examining the effects of dronedarone in patients receiving other QT prolonging drugs, coadministration of such drugs may result in additive QT prolongation.
Droperidol: (Major) Droperidol should be administered with extreme caution to patients receiving other agents that may prolong the QT interval. Droperidol administration is associated with an established risk for QT prolongation and torsades de pointes (TdP). Any drug known to have potential to prolong the QT interval should not be coadministered with droperidol. Drugs with a possible risk for QT prolongation and TdP that should be used cautiously with droperidol include haloperidol.
Duloxetine: (Moderate) Duloxetine is a moderate inhibitor of CYP2D6. Substantial increases in concentrations of antipsychotics primarily metabolized via CYP2D6, such as haloperidol may also occur. Haloperidol is associated with a possible risk of QT prolongation and should be used cautiously with CYP2D6 inhibitors such as duloxetine.
Dutasteride; Tamsulosin: (Moderate) Use caution when administering tamsulosin with a moderate CYP2D6 inhibitor such as haloperidol. Tamsulosin is extensively metabolized by CYP2D6 hepatic enzymes. In clinical evaluation, concomitant treatment with a strong CYP2D6 inhibitor resulted in increases in tamsulosin exposure; interactions with moderate CYP2D6 inhibitors have not been evaluated. If concomitant use in necessary, monitor patient closely for increased side effects.
Efavirenz: (Major) Coadministration of efavirenz and haloperidol may increase the risk for QT prolongation and torsade de pointes (TdP). QT prolongation has been observed with use of efavirenz. Although data are limited, the manufacturer of efavirenz recommends an alternative antiretroviral be considered for patients receiving medications with a known risk for TdP. QT prolongation and TdP have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. In addition, efavirenz is a substrate and inducer of CYP3A4, one of the isoenzymes responsible for the metabolism of haloperidol. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and substrates or inhibitors of CYP3A4. Because this interaction may be unpredictable, it is advisable to closely monitor for adverse events or a decrease in efficacy when these medications are co-administered.
Efavirenz; Emtricitabine; Tenofovir: (Major) Coadministration of efavirenz and haloperidol may increase the risk for QT prolongation and torsade de pointes (TdP). QT prolongation has been observed with use of efavirenz. Although data are limited, the manufacturer of efavirenz recommends an alternative antiretroviral be considered for patients receiving medications with a known risk for TdP. QT prolongation and TdP have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. In addition, efavirenz is a substrate and inducer of CYP3A4, one of the isoenzymes responsible for the metabolism of haloperidol. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and substrates or inhibitors of CYP3A4. Because this interaction may be unpredictable, it is advisable to closely monitor for adverse events or a decrease in efficacy when these medications are co-administered.
Efavirenz; Lamivudine; Tenofovir Disoproxil Fumarate: (Major) Coadministration of efavirenz and haloperidol may increase the risk for QT prolongation and torsade de pointes (TdP). QT prolongation has been observed with use of efavirenz. Although data are limited, the manufacturer of efavirenz recommends an alternative antiretroviral be considered for patients receiving medications with a known risk for TdP. QT prolongation and TdP have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. In addition, efavirenz is a substrate and inducer of CYP3A4, one of the isoenzymes responsible for the metabolism of haloperidol. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and substrates or inhibitors of CYP3A4. Because this interaction may be unpredictable, it is advisable to closely monitor for adverse events or a decrease in efficacy when these medications are co-administered.
Elbasvir; Grazoprevir: (Moderate) Administering haloperidol with elbasvir; grazoprevir may result in elevated haloperidol plasma concentrations. Haloperidol is a substrate of CYP3A; grazoprevir is a weak CYP3A inhibitor. If these drugs are used together, closely monitor for signs of adverse events.
Eliglustat: (Major) Use great caution when coadministering haloperidol and eliglustat due to the risk of serious adverse events such as QT prolongation and cardiac arrhythmias. If concurrent use is necessary, consider reducing the dosage of haloperidol and titrating to clinical effect. Although haloperidol's impact on eliglustat is unclear, it may be prudent to reduce the eliglustat dosage to 84 mg PO once daily in extensive or intermediate CYP2D6 metabolizers (EMs or IMs). If eliglustat and haloperidol are taken together, concurrent use of a strong or moderate CYP3A inhibitor should be avoided. Eliglustat is a CYP2D6 and CYP3A substrate that is predicted to cause PR, QRS, and/or QT prolongation at significantly elevated plasma concentrations; it is also a CYP2D6 inhibitor. Haloperidol is primarily metabolized by CYP2D6; however, its inhibitory effects are unclear. Some pharmacokinetic data suggests that haloperidol may inhibit CYP2D6 and CYP3A4, while other data suggests the risk of clinically significant inhibition is low. Regardless, haloperidol has been associated with QT prolongation and torsade de pointes (TdP). Coadministration of haloperidol and eliglustat may result in additive effects on the QT interval and, potentially, increased plasma concentrations of one or both drugs, further increasing the risk of serious adverse events (e.g., QT prolongation and cardiac arrhythmias).
Emtricitabine; Rilpivirine; Tenofovir alafenamide: (Major) Supratherapeutic doses of rilpivirine (75 to 300 mg/day) have caused QT prolongation;

caution is advised when administering rilpivirine with other drugs that may prolong the QT or PR interval, such as haloperidol. QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation.
Emtricitabine; Rilpivirine; Tenofovir disoproxil fumarate: (Major) Supratherapeutic doses of rilpivirine (75 to 300 mg/day) have caused QT prolongation; caution is advised when administering rilpivirine with other drugs that may prolong the QT or PR interval, such as haloperidol. QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation.
Enalapril; Felodipine: (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Enalapril; Hydrochlorothiazide, HCTZ: (Major) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. The risk of QT prolongation may also be increased during use of haloperidol and medications known to cause electrolyte imbalance such as thiazide diuretics.
Encainide: (Major) Encainide is significantly metabolized by CYP2D6 isoenzymes. Caution is recommended when administering encainide with CYP2D6 inhibitors, such as haloperidol, since encainide exhibits a narrow therapeutic range and large increases in serum concentrations may be associated with severe adverse reactions.
Encorafenib: (Major) Avoid coadministration of encorafenib and haloperidol due to QT prolongation. Encorafenib is associated with dose-dependent prolongation of the QT interval. QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation.
Enflurane: (Major) QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval. Drugs with a possible risk for QT prolongation and TdP that should be used cautiously and with close monitoring with haloperidol include halogenated anesthetics.
Entacapone: (Major) COMT inhibitors should be given cautiously with other agents that cause CNS depression, including haloperidol, due to the possibility of additive sedation.
Enzalutamide: (Moderate) Monitor for decreased efficacy of haloperidol if coadministration with enzalutamide is necessary. Haloperidol is a CYP3A4 substrate and enzalutamide is a strong CYP3A4 inducer. Coadministration with another strong CYP3A4 inducer decreased haloperidol plasma concentrations by a mean of 70% and increased mean scores on the Brief Psychiatric Rating Scale from baseline.
Epinephrine: (Major) Use of epinephrine to treat droperidol or haloperidol -induced hypotension can result in a paradoxical lowering of blood pressure due to droperidol's alpha-blocking effects. Avoid using epinephrine concurrently with droperidol and haloperidol.
Eplerenone: (Moderate) In general, haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Epoprostenol: (Moderate) In general, haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Eprosartan: (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Eprosartan; Hydrochlorothiazide, HCTZ: (Major) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. The risk of QT prolongation may also be increased during use of haloperidol and medications known to cause electrolyte imbalance such as thiazide diuretics. (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Eribulin: (Major) QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval, including eribulin. ECG monitoring is recommended; closely monitor the patient for QT interval prolongation.
Erythromycin: (Major) Due to the potential for QT prolongation and torsade de pointes (TdP), caution is advised when administering erythromycin with haloperidol. It is prudent to use caution and carefully weighing the risks and benefits of these agents versus alternative treatment options. Erythromycin has an established risk for QT prolongation and TdP. QT prolongation and TdP have also been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) of haloperidol may be associated with a higher risk of QT prolongation. In addition, inhibition of CYP3A4 by eythromycin may result in elevated haloperidol concentrations, thereby increasing the risk of adverse effects, including QT prolongation.
Erythromycin; Sulfisoxazole: (Major) Due to the potential for QT prolongation and torsade de pointes (TdP), caution is advised when administering erythromycin with haloperidol. It is prudent to use caution and carefully weighing the risks and benefits of these agents versus alternative treatment options. Erythromycin has an established risk for QT prolongation and TdP. QT prolongation and TdP have also been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) of haloperidol may be associated with a higher risk of QT prolongation. In addition, inhibition of CYP3A4 by eythromycin may result in elevated haloperidol concentrations, thereby increasing the risk of adverse effects, including QT prolongation.
Escitalopram: (Major) Escitalopram has been associated with QT prolongation. Coadministration with other drugs that have a possible risk for QT prolongation and torsade de pointes (TdP), such as haloperidol, should be done with caution and close monitoring. In addition, escitalopram modestly inhibits CYP2D6. This can result in increased concentrations of haloperidol. Clinically important adverse reactions associated with antipsychotic use, such as extrapyramidal symptoms, are possible.
Esmolol: (Moderate) Haloperidol should be used cautiously with esmolol due to the possibility of additive hypotension.
Estazolam: (Moderate) Haloperidol can potentiate the actions of other CNS depressants, such as benzodiazepines, Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.
Eszopiclone: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as anxiolytics, sedatives, and hypnotics, and they should be used cautiously in combination.
Ethacrynic Acid: (Major) QT prolongation has been observed during haloperidol treatment. Use of haloperidol and medications known to cause electrolyte imbalance may increase the risk of QT prolongation. Therefore, caution is advisable during concurrent use of haloperidol and loop diuretics. In general, haloperidol should also be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Ethanol: (Major) In general, patients should avoid alcohol during haloperidol treatment. Haloperidol may impair alertness, mental and/or physical abilities, and cause hypotension. These effects may be potentiated by alcohol. Patients should be warned of the risks of sedation and hypotension and advised of associated precautions.
Ethosuximide: (Moderate) Concomitant use of ethosuximide with haloperidol can lower the seizure threshold and reduce the effectiveness of ethosuximide as an anticonvulsant. Additive CNS effects, such as drowsiness, may also occur.
Etomidate: (Major) Haloperidol can potentiate the actions of other CNS depressants such as sedatives and hypnotics. Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.
Everolimus: (Moderate) Monitor for an increase in haloperidol-related adverse reactions if coadministration with everolimus is necessary. Haloperidol is a CYP3A4 and CYP2D6 substrate. Everolimus is a weak CYP3A4 inhibitor as well as a CYP2D6 inhibitor; concomitant use may increase plasma concentrations of haloperidol.
Ezogabine: (Major) Use with caution due to the potential for additive effects on the QT interval. Haloperidol has been specifically established to have a causal association with QT prolongation and torsade de pointes (TdP). Ezogabine has been associated with QT prolongation. The manufacturer of ezogabine recommends that the QT interval (ECG) be monitored in patients receiving other medications known to cause QT prolongation along with ezogabine.
Felodipine: (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Fentanyl: (Moderate) Concomitant use of fentanyl with other central nervous system (CNS) depressants, such as haloperidol, can potentiate the effects of fentanyl and may lead to additive CNS or respiratory depression, profound sedation, or coma. Prior to concurrent use of fentanyl in patients taking a CNS depressant, assess the level of tolerance to CNS depression that has developed, the duration of use, and the patient's overall

response to treatment. Consider the patient's use of alcohol or illicit drugs. If these agents are used together, a reduced dosage of fentanyl and/or haloperidol is recommended. Carefully monitor the patient for hypotension, CNS depression, and respiratory depression. Carbon dioxide retention from opioid-induced respiratory depression can exacerbate the sedating effects of opioids.
Fexofenadine; Pseudoephedrine: (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol directly counteract the effects of pseudoephedrine and can counter the desired pharmacologic effect. They also can be used to treat excessive pseudoephedrine-induced hypertension.
Fingolimod: (Major) QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval. Drugs with a possible risk for QT prolongation and TdP that should be used cautiously with haloperidol include fingolimod. Fingolimod initiation results in decreased heart rate and may prolong the QT interval. After the first fingolimod dose, overnight monitoring with continuous ECG in a medical facility is advised for patients taking QT prolonging drugs with a known risk of torsades de pointes (TdP). Fingolimod has not been studied in patients treated with drugs that prolong the QT interval, but drugs that prolong the QT interval have been associated with cases of TdP in patients with bradycardia.
Flecainide: (Major) Due to the potential for QT prolongation and torsade de pointes (TdP), caution is advised when administering haloperidol with flecainide. QT prolongation and TdP have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. Flecainide, a Class IC antiarrhythmic, is also associated with a possible risk for QT prolongation and/or TdP; flecainide increases the QT interval, but largely due to prolongation of the QRS interval. Although causality for TdP has not been established for flecainide, patients receiving concurrent drugs which have the potential for QT prolongation may have an increased risk of developing proarrhythmias. In addition, flecainide is significantly metabolized by CYP2D6, and haloperidol is a CYP2D6 inhibitor. Coadministration may result in elevated flecainide serum concentrations.
Fluconazole: (Severe) The concurrent use of fluconazole with drugs that are associated with QT prolongation and are CYP3A4 substrates, such as haloperidol, is contraindicated. Fluconazole has been associated with QT prolongation; QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Additionally, haloperidol is primarily metabolized by CYP2D6. However, in patients that are lacking in CYP2D6 enzyme activity (slow metabolizers), the CYP3A4 enzyme may play a larger role in haloperidol metabolism. Fluconazole is a CYP2D6 and CYP3A4 inhibitor; therefore, concurrent use may increase haloperidol concentrations. Elevated haloperidol concentrations occurring through inhibition of CYP2D6 or CYP3A4 may increase the risk of adverse effects, including QT prolongation.
Fluoxetine: (Major) Fluoxetine is a potent inhibitor of CYP2D6 and its metabolite is a moderate CYP3A4 inhibitor, which may result in decreased clearance of antipsychotics that are CYP2D6 and CYP3A4 substrates including haloperidol. Decrease metabolism of haloperidol can result in adverse effects associated with haloperidol use including dizziness, impaired psychomotor performance, and extrapyramidal symptoms. In addition, haloperidol is associated with a risk for QT prolongation and TdP, and should be used cautiously with potent CYP2D6 inhibitors such as fluoxetine. Because symptoms consistent with elevated haloperidol levels have been observed during co-administration of SSRIs, patients receiving these combinations should be carefully monitored for adverse effects. The effects of fluoxetine on hepatic metabolism of interacting drugs may persist for several weeks after discontinuation of fluoxetine because of its long elimination half-life.
Fluoxetine; Olanzapine: (Major) Fluoxetine is a potent inhibitor of CYP2D6 and its metabolite is a moderate CYP3A4 inhibitor, which may result in decreased clearance of antipsychotics that are CYP2D6 and CYP3A4 substrates including haloperidol. Decrease metabolism of haloperidol can result in adverse effects associated with haloperidol use including dizziness, impaired psychomotor performance, and extrapyramidal symptoms. In addition, haloperidol is associated with a risk for QT prolongation and TdP, and should be used cautiously with potent CYP2D6 inhibitors such as fluoxetine. Because symptoms consistent with elevated haloperidol levels have been observed during co-administration of SSRIs, patients receiving these combinations should be carefully monitored for adverse effects. The effects of fluoxetine on hepatic metabolism of interacting drugs may persist for several weeks after discontinuation of fluoxetine because of its long elimination half-life. (Major) QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval, including olanzapine. Coadministration may increase the risk of adverse effects such as drowsiness, dizziness, orthostatic hypotension, anticholinergic effects, extrapyramidal symptoms, neuroleptic malignant syndrome, or seizures. The likelihood of these pharmacodynamic interactions varies based upon the individual properties of the co-administered antipsychotic agent. Although the incidence of tardive dyskinesia from combination antipsychotic therapy has not been established and data are very limited, the risk appears to be increased during use of a conventional and atypical antipsychotic versus use of a conventional antipsychotic alone.
Fluphenazine: (Moderate) Fluphenazine, a phenothiazine, is associated with a possible risk for QT prolongation. Haloperidol is associated with a possible risk for QT prolongation and TdP. Coadministration may increase the risk of adverse effects such as drowsiness, dizziness, orthostatic hypotension, anticholinergic effects, extrapyramidal symptoms, neuroleptic malignant syndrome, or seizures. The likelihood of these pharmacodynamic interactions varies based upon the individual properties of the co-administered antipsychotic agent. Although the incidence of tardive dyskinesia from combination antipsychotic therapy has not been established and data are very limited, the risk appears to be increased during use of a conventional and atypical antipsychotic versus use of a conventional antipsychotic alone.
Flurazepam: (Moderate) Haloperidol can potentiate the actions of other CNS depressants, such as benzodiazepines, Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.
Fluvoxamine: (Major) There may be an increased risk for QT prolongation, torsade de pointes (TdP), or elevated haloperidol concentrations during concurrent use of fluvoxamine and haloperidol. Cases of QT prolongation and TdP have been reported during postmarketing use of fluvoxamine. QT prolongation and TdP have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. In addition, haloperidol is metabolized by CYP2D6 and CYP3A4. Fluvoxamine is a moderate inhibitor of CYP3A4 and may decrease haloperidol metabolism. Symptoms of haloperidol excess have been observed in the patients receiving haloperidol and fluvoxamine together. Elevated haloperidol concentrations occurring through inhibition of cytochrome P450 pathways may increase the risk of haloperidol-induced adverse effects, including QT prolongation or extrapyramidal symptoms.
Food: (Major) Haloperidol is sometimes used to treat emesis due to cannabis use; in this case, interactions are not expected; however, patients should be warned about sedation and other potential effects. Patients on chronic haloperidol therapy for psychiatric disorders should avoid use of marijuana. It is recommended that patients avoid the use of marijuana, by any route, if they are treated for a psychiatric history, including psychosis and bipolar disorder, as the cannabinoids (the psychoactive ingredients, such as THC) in marijuana can produce psychotoxic effects and may exacerbate psychiatric disorders. A high frequency of use and use of products with high-potency of THC are potential risk factors for psychiatric effects. Additionally, additive CNS effects, such as sedation or CNS depression are possible. Clinical studies suggest that cannabis use may reduce the efficacy of some antipsychotic drugs. In addition, several cannabinoids in marijuana appear to influence the activity of CYP enzymes and P-glycoprotein, which may alter the concentrations of antipsychotics and influence either safety or efficacy, For example, the smoking of marijuana influences the metabolism of some medications in a manner similar to tobacco by inducing CYP1A2.
Fosamprenavir: (Moderate) Fosamprenavir is an inhibitor of CYP3A4. CYP3A4 is one of the isoenzymes responsible for the metabolism of haloperidol. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and inhibitors of CYP3A4. Elevated haloperidol concentrations occurring through inhibition of CYP3A4 may increase the risk of adverse effects, including QT prolongation. Until more data are available, it is advisable to closely monitor for adverse events when these medications are co-administered.
Foscarnet: (Major) When possible, avoid concurrent use of foscarnet with other drugs known to prolong the QT interval, such as haloperidol. Foscarnet has been associated with postmarketing reports of both QT prolongation and torsade de pointes (TdP). QT prolongation and TdP have also been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. If these drugs are administered together, obtain an electrocardiogram and electrolyte concentrations before and periodically during treatment.
Fosinopril; Hydrochlorothiazide, HCTZ: (Major) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. The risk of QT prolongation may also be increased during use of haloperidol and medications known to cause electrolyte imbalance such as thiazide diuretics.
Fospropofol: (Major) Haloperidol can potentiate the actions of other CNS depressants such as general anesthetics. Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.

Furosemide: (Major) QT prolongation has been observed during haloperidol treatment. Use of haloperidol and medications known to cause electrolyte imbalance may increase the risk of QT prolongation. Therefore, caution is advisable during concurrent use of haloperidol and loop diuretics. In general, haloperidol should also be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Gabapentin: (Moderate) Antipsychotics that may enhance the CNS depressive effects of gabapentin, such as drowsiness or dizziness, include haloperidol. Patients should limit activity until they are aware of how coadministration affects them.
Ganirelix: (Moderate) In the absence of relevant data and as a precaution, drugs that cause hyperprolactinemia, such as antipsychotics, should not be administered concomitantly with gonadotropin releasing hormone analogs since hyperprolactinemia downregulates the number of pituitary GnRH receptors.
Gefitinib: (Moderate) Gefitinib is an inhibitor of CYP2D6, the primary isoenzyme responsible for the metabolism of haloperidol. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and inhibitors of CYP2D6. Until more data are available, it is advisable to closely monitor for adverse events when these medications are co-administered.
Gemifloxacin: (Major) Due to an increased risk for QT prolongation and torsade de pointes (TdP), caution is advised when administering haloperidol with gemifloxacin. QT prolongation and TdP have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. Gemifloxacin may also prolong the QT interval in some patients with the maximal change in the QTc interval occurring approximately 5 to 10 hours following oral administration. The likelihood of QTc prolongation may increase with increasing dose of gemifloxacin; therefore, the recommended dose should not be exceeded especially in patients with renal or hepatic impairment where the Cmax and AUC are slightly higher.
Gemtuzumab Ozogamicin: (Major) Use gemtuzumab ozogamicin and haloperidol together with caution due to the potential for additive QT interval prolongation and risk of torsade de pointes (TdP). If these agents are used together, obtain an ECG and serum electrolytes prior to the start of gemtuzumab and as needed during treatment. Although QT interval prolongation has not been reported with gemtuzumab, it has been reported with other drugs that contain calicheamicin. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation.
Glycerol Phenylbutyrate: (Moderate) Haloperidol may induce elevated blood ammonia concentrations. Use caution and monitor ammonia concentrations closely if co-administration of haloperidol and glycerol phenylbutyrate is necessary.
Glycopyrrolate: (Moderate) Coadministration of glycopyrrolate with haloperidol may decrease haloperidol serum concentrations, which may lead to worsening of psychiatric symptoms and the development of tardive dyskinesia. If coadministration is necessary, closely monitor patient.
Glycopyrrolate; Formoterol: (Moderate) Coadministration of glycopyrrolate with haloperidol may decrease haloperidol serum concentrations, which may lead to worsening of psychiatric symptoms and the development of tardive dyskinesia. If coadministration is necessary, closely monitor patient.
Goserelin: (Major) QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. Due to the risk of additive QT prolongation and potential for serious arrhythmias, the concurrent use of haloperidol with androgen deprivation therapy (e.g., goserelin) should be approached with caution. Androgen deprivation therapy prolongs the QT interval. In addition, in the absence of relevant data and as a precaution, drugs that cause hyperprolactinemia (e.g., some antipsychotics) should not be administered concomitantly with goserelin since hyperprolactinemia down-regulates the number of pituitary GnRH receptors.
Granisetron: (Major) Granisetron has been associated with QT prolongation. According to the manufacturer, the use of granisetron in patients concurrently treated with drugs known to prolong the QT interval (e.g., haloperidol) and/or are arrhythmogenic, may result in clinical consequences.
Guaifenesin; Hydrocodone: (Moderate) Concomitant use of hydrocodone with haloperidol may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of haloperidol could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If haloperidol is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Haloperidol is a moderate inhibitor of CYP2D6.
Guaifenesin; Hydrocodone; Pseudoephedrine: (Moderate) Concomitant use of hydrocodone with haloperidol may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of haloperidol could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If haloperidol is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Haloperidol is a moderate inhibitor of CYP2D6. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol directly counteract the effects of pseudoephedrine and can counter the desired pharmacologic effect. They also can be used to treat excessive pseudoephedrine-induced hypertension.
Guaifenesin; Phenylephrine: (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol, directly counteract the effects of phenylephrine and can counter the desired pharmacologic effect. They also can be used to treat excessive phenylephrine-induced hypertension.
Guaifenesin; Pseudoephedrine: (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol directly counteract the effects of pseudoephedrine and can counter the desired pharmacologic effect. They also can be used to treat excessive pseudoephedrine-induced hypertension.
Guanabenz: (Moderate) Disturbances of orthostatic regulation (e.g., orthostatic hypotension, dizziness, fatigue) and additive sedation may occur in patients receiving concomitant clonidine and antipsychotics. Also, based on observations in patients in a state of alcoholic delirium, high intravenous doses of clonidine may increase the arrhythmogenic potential (QT prolongation, ventricular fibrillation) of high intravenous doses of haloperidol. A causal relationship and relevance for clonidine oral tablets have not been established.
Guanfacine: (Moderate) Disturbances of orthostatic regulation (e.g., orthostatic hypotension, dizziness, fatigue) and additive sedation may occur in patients receiving concomitant clonidine and antipsychotics. Also, based on observations in patients in a state of alcoholic delirium, high intravenous doses of clonidine may increase the arrhythmogenic potential (QT prolongation, ventricular fibrillation) of high intravenous doses of haloperidol. A causal relationship and relevance for clonidine oral tablets have not been established.
Halofantrine: (Severe) Halofantrine is considered to have a well-established risk for QT prolongation and torsades de pointes. Halofantrine should be avoided in patients receiving drugs which may induce QT prolongation, such as haloperidol and, droperidol.
Halogenated Anesthetics: (Major) QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval. Drugs with a possible risk for QT prolongation and TdP that should be used cautiously and with close monitoring with haloperidol include halogenated anesthetics.
Halothane: (Major) QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval. Drugs with a possible risk for QT prolongation and TdP that should be used cautiously and with close monitoring with haloperidol include halogenated anesthetics.
Histrelin: (Major) Consider periodic monitoring of EGCs for QT prolongation and monitor electrolytes if coadministration of histrelin and haloperidol is necessary; correct any electrolyte abnormalities. Androgen deprivation therapy (e.g., histrelin) prolongs the QT interval; the risk may be increased with the concurrent use of drugs that may prolong the QT interval. Prolongation of the QT interval and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation.
Homatropine; Hydrocodone: (Moderate) Concomitant use of hydrocodone with haloperidol may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and

consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of haloperidol could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If haloperidol is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Haloperidol is a moderate inhibitor of CYP2D6.

Hydantoins: (Major) Haloperidol is metabolized in the liver; hydantoin anticonvulsants are known to induce certain hepatic enzymes. Clinicians should monitor for reduced haloperidol effectiveness if a hydantoin is used concurrently. Conversely, the discontinuation of these drugs may produce an increase in haloperidol concentrations. Additionally, antipsychotic use may lower the seizure threshold in patients receiving anticonvulsants, although the risk is less with haloperidol than with the phenothiazines. Additional CNS depression may occur when haloperidol is given with anticonvulsant drugs.

Hydralazine; Hydrochlorothiazide, HCTZ: (Major) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. The risk of QT prolongation may also be increased during use of haloperidol and medications known to cause electrolyte imbalance such as thiazide diuretics.

Hydrochlorothiazide, HCTZ: (Major) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. The risk of QT prolongation may also be increased during use of haloperidol and medications known to cause electrolyte imbalance such as thiazide diuretics.

Hydrochlorothiazide, HCTZ; Irbesartan: (Major) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. The risk of QT prolongation may also be increased during use of haloperidol and medications known to cause electrolyte imbalance such as thiazide diuretics. (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.

Hydrochlorothiazide, HCTZ; Lisinopril: (Major) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. The risk of QT prolongation may also be increased during use of haloperidol and medications known to cause electrolyte imbalance such as thiazide diuretics.

Hydrochlorothiazide, HCTZ; Losartan: (Major) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. The risk of QT prolongation may also be increased during use of haloperidol and medications known to cause electrolyte imbalance such as thiazide diuretics. (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.

Hydrochlorothiazide, HCTZ; Methyldopa: (Major) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. The risk of QT prolongation may also be increased during use of haloperidol and medications known to cause electrolyte imbalance such as thiazide diuretics. (Moderate) Disturbances of orthostatic regulation (e.g., orthostatic hypotension, dizziness, fatigue) and additive sedation may occur in patients receiving concomitant clonidine and antipsychotics. Also, based on observations in patients in a state of alcoholic delirium, high intravenous doses of clonidine may increase the arrhythmogenic potential (QT prolongation, ventricular fibrillation) of high intravenous doses of haloperidol. A causal relationship and relevance for clonidine oral tablets have not been established.

Hydrochlorothiazide, HCTZ; Metoprolol: (Major) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. The risk of QT prolongation may also be increased during use of haloperidol and medications known to cause electrolyte imbalance such as thiazide diuretics. (Moderate) Monitor for increased metoprolol adverse reactions including bradycardia and hypotension during coadministration. A dosage reduction for metoprolol may be needed based on response. Concurrent use may increase metoprolol exposure. Metoprolol is a CYP2D6 substrate; haloperidol is a moderate CYP2D6 inhibitor. In the presence of another moderate CYP2D6 inhibitor, the AUC of metoprolol was increased by 3.29-fold with no effect on the cardiovascular response to metoprolol.

Hydrochlorothiazide, HCTZ; Moexipril: (Major) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. The risk of QT prolongation may also be increased during use of haloperidol and medications known to cause electrolyte imbalance such as thiazide diuretics.

Hydrochlorothiazide, HCTZ; Olmesartan: (Major) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. The risk of QT prolongation may also be increased during use of haloperidol and medications known to cause electrolyte imbalance such as thiazide diuretics. (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.

Hydrochlorothiazide, HCTZ; Propranolol: (Major) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. The risk of QT prolongation may also be increased during use of haloperidol and medications known to cause electrolyte imbalance such as thiazide diuretics. (Moderate) Haloperidol should be used cautiously with propranolol due to the possibility of additive hypotension and increased concentrations of propranolol. Propranolol is significantly metabolized by CYP2D6 isoenzymes. A case report of 3 severe hypotension episodes (2 requiring cardiopulmonary resuscitation) has been reported in one 48 year old woman when propranolol and haloperidol have been coadministered. Additive hypotensive effects and haloperidol-mediated CYP2D6 inhibition may have contributed to this interaction.

Hydrochlorothiazide, HCTZ; Quinapril: (Major) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. The risk of QT prolongation may also be increased during use of haloperidol and medications known to cause electrolyte imbalance such as thiazide diuretics.

Hydrochlorothiazide, HCTZ; Spironolactone: (Major) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. The risk of QT prolongation may also be increased during use of haloperidol and medications known to cause electrolyte imbalance such as thiazide diuretics. (Moderate) In general, haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.

Hydrochlorothiazide, HCTZ; Telmisartan: (Major) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. The risk of QT prolongation may also be increased during use of haloperidol and medications known to cause electrolyte imbalance such as thiazide diuretics. (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.

Hydrochlorothiazide, HCTZ; Triamterene: (Major) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. The risk of QT prolongation may also be increased during use of haloperidol and medications known to cause electrolyte imbalance such as thiazide diuretics. (Moderate) In general, haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.

Hydrochlorothiazide, HCTZ; Valsartan: (Major) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. The risk of QT prolongation may also be increased during use of haloperidol and medications known to cause electrolyte imbalance such as thiazide diuretics. (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.

Hydrocodone: (Moderate) Concomitant use of hydrocodone with haloperidol may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of haloperidol could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If haloperidol is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Haloperidol is a moderate inhibitor of CYP2D6.

Hydrocodone; Ibuprofen: (Moderate) Concomitant use of hydrocodone with haloperidol may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of haloperidol could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If haloperidol is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Haloperidol is a moderate inhibitor of CYP2D6.

Hydrocodone; Phenylephrine: (Moderate) Concomitant use of hydrocodone with haloperidol may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of haloperidol could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If haloperidol is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Haloperidol is a moderate inhibitor of CYP2D6. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol, directly counteract the effects of phenylephrine and can counter the desired pharmacologic effect. They also can be used to treat excessive phenylephrine-induced hypertension.
Hydrocodone; Potassium Guaiacolsulfonate: (Moderate) Concomitant use of hydrocodone with haloperidol may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of haloperidol could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If haloperidol is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Haloperidol is a moderate inhibitor of CYP2D6.
Hydrocodone; Potassium Guaiacolsulfonate; Pseudoephedrine: (Moderate) Concomitant use of hydrocodone with haloperidol may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of haloperidol could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If haloperidol is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Haloperidol is a moderate inhibitor of CYP2D6. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol directly counteract the effects of pseudoephedrine and can counter the desired pharmacologic effect. They also can be used to treat excessive pseudoephedrine-induced hypertension.
Hydrocodone; Pseudoephedrine: (Moderate) Concomitant use of hydrocodone with haloperidol may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of haloperidol could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If haloperidol is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Haloperidol is a moderate inhibitor of CYP2D6. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol directly counteract the effects of pseudoephedrine and can counter the desired pharmacologic effect. They also can be used to treat excessive pseudoephedrine-induced hypertension.
Hydromorphone: (Moderate) Concomitant use of hydromorphone with other central nervous system (CNS) depressants can potentiate the effects of hydromorphone and may lead to additive CNS or respiratory depression, profound sedation, or coma. Examples of drugs associated with CNS depression include haloperidol. Prior to concurrent use of hydromorphone in patients taking a CNS depressant, assess the level of tolerance to CNS depression that has developed, the duration of use, and the patient's overall response to treatment. Consider the patient's use of alcohol or illicit drugs. If hydromorphone is used concurrently with a CNS depressant, a reduced dosage of hydromorphone and/or the CNS depressant is recommended; start with one-third to one-half of the estimated hydromorphone starting dose when using hydromorphone extended-release tablets. Carefully monitor the patient for hypotension, CNS depression, and respiratory depression. Carbon dioxide retention from opioid-induced respiratory depression can exacerbate the sedating effects of opioids.
Hydroxychloroquine: (Major) Avoid coadministration of hydroxychloroquine and haloperidol. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. QT prolongation and TdP have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. Additionally, hydroxychloroquine is an inhibitor of CYP2D6, one of the isoenzymes responsible for the metabolism of haloperidol. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and inhibitors of CYP2D6. Elevated haloperidol concentrations occurring through inhibition of CYP2D6 may increase the risk of adverse effects, including QT prolongation.
Hydroxyzine: (Major) Haloperidol should be used cautiously and with close monitoring with hydroxyzine. Post-marketing data indicate that hydroxyzine causes QT prolongation and Torsade de Pointes (TdP). QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval.
Hyoscyamine: (Moderate) Additive adverse effects resulting from cholinergic blockade may occur when hyoscyamine is administered concomitantly with haloperidol.
Hyoscyamine; Methenamine; Methylene Blue; Phenyl Salicylate; Sodium Biphosphate: (Moderate) Additive adverse effects resulting from cholinergic blockade may occur when hyoscyamine is administered concomitantly with haloperidol.
Ibuprofen; Oxycodone: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as opiate agonists. Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.
Ibuprofen; Pseudoephedrine: (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol directly counteract the effects of pseudoephedrine and can counter the desired pharmacologic effect. They also can be used to treat excessive pseudoephedrine-induced hypertension.
Ibutilide: (Major) QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval. Ibutilide administration can cause QT prolongation and torsades de pointes (TdP); proarrhythmic events should be anticipated. The potential for proarrhythmic events with ibutilide increases with the coadministration of other drugs that prolong the QT interval.
Idelalisib: (Major) Avoid concomitant use of idelalisib, a strong CYP3A inhibitor, with haloperidol, a CYP3A substrate, as haloperidol toxicities may be significantly increased. The AUC of a sensitive CYP3A substrate was increased 5.4-fold when coadministered with idelalisib.
Iloperidone: (Major) Haloperidol should be avoided in combination with iloperidone, due to duplicative antipsychotic effects and the potential for additive effects on the QT interval. Haloperidol is associated with a possible risk for QT prolongation and torsade de pointes (TdP) and iloperidone has been associated with QT prolongation. Coadministration may increase the risk of adverse effects such as drowsiness, dizziness, orthostatic hypotension, anticholinergic effects, extrapyramidal symptoms, neuroleptic malignant syndrome, or seizures. Although the incidence of tardive dyskinesia from combination antipsychotic therapy has not been established and data are very limited, the risk appears to be increased during use of a conventional and atypical antipsychotic versus use of a conventional antipsychotic alone.
Iloprost: (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Imatinib: (Moderate) Imatinib, STI-571 is an inhibitor of CYP2D6 and CYP3A4, the isoenzymes responsible for the metabolism of haloperidol. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and inhibitors of CYP3A4 or CYP2D6. Until more data are available, it is advisable to closely monitor for adverse events when these medications are co-administered.
Indacaterol; Glycopyrrolate: (Moderate) Coadministration of glycopyrrolate with haloperidol may decrease haloperidol serum concentrations, which may lead to worsening of psychiatric symptoms and the development of tardive dyskinesia. If coadministration is necessary, closely monitor patient.
Indinavir: (Moderate) Indinavir is a substrate and inhibitor of CYP3A4, one of the isoenzymes responsible for the metabolism of haloperidol. Mild to

moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and substrates or inhibitors of CYP3A4. Until more data are available, it is advisable to closely monitor for adverse events when these medications are co-administered.
Indocyanine Green: (Moderate) Haloperidol may increase the clearance of indocyanine green. The half-life of indocyanine green was lower in patients taking the drugs concomitantly compared to patients with normal and abnormal liver function taking no concomitant medications. The mechanism of interaction is unclear; those proposed in the medical literature include increased indocyanine green uptake by the liver cell, enhanced binding by specific hepatic carrier proteins, or more rapid excretion into bile.
Indomethacin: (Minor) In a small study, during concomitant administration of haloperidol with indomethacin, adverse reactions, such as drowsiness and other effects, to haloperidol appeared to be intensified. Although more data are needed to confirm these findings, clinicians should administer indomethacin to patients stabilized on haloperidol cautiously. The effect of other NSAIDs on haloperidol are unknown.
Inotuzumab Ozogamicin: (Major) Avoid coadministration of inotuzumab ozogamicin with haloperidol due to the potential for additive QT interval prolongation and risk of torsade de pointes (TdP). If coadministration is unavoidable, obtain an ECG and serum electrolytes prior to the start of treatment, after treatment initiation, and periodically during treatment. Inotuzumab has been associated with QT interval prolongation. QT prolongation and TdP have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation.
Irbesartan: (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Isavuconazonium: (Moderate) Concomitant use of isavuconazonium with haloperidol may result in increased serum concentrations of haloperidol. Haloperidol is a substrate of the hepatic isoenzyme CYP3A4; isavuconazole, the active moiety of isavuconazonium, is a moderate inhibitor of this enzyme. Caution and close monitoring are advised if these drugs are used together.
Isoflurane: (Major) QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval. Drugs with a possible risk for QT prolongation and TdP that should be used cautiously and with close monitoring with haloperidol include halogenated anesthetics.
Isoniazid, INH: (Moderate) Isoniazid, INH is a potent inhibitor of CYP3A4 and a mild inhibitor of CYP2D6, the isoenzymes responsible for the metabolism of haloperidol. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and substrates or inhibitors of CYP3A4 or CYP2D6. Elevated haloperidol concentrations occurring through inhibition of CYP2D6 or CYP3A4 may increase the risk of adverse effects, including QT prolongation. Until more data are available, it is advisable to closely monitor for adverse events when these medications are co-administered.
Isoniazid, INH; Pyrazinamide, PZA; Rifampin: (Major) Limited data suggest that rifampin, a potent CYP inducer, can increase the metabolism and/or reduce the bioavailability of haloperidol. In one small study (n=12), plasma levels of haloperidol were decreased by a mean of 70% and mean scores on the Brief Psychiatric Rating Scale (BPRS) were increased from baseline during concurrent use of rifampin. Discontinuation of rifampin has resulted in a mean 3.3-fold increase in haloperidol concentrations in some instances. Haloperidol dosage adjustments should be made as needed when rifampin is added or discontinued. Prolonged use of CYP inducers such as rifampin in patients receiving haloperidol has resulted in significant reductions in haloperidol plasma concentrations. (Moderate) Isoniazid, INH is a potent inhibitor of CYP3A4 and a mild inhibitor of CYP2D6, the isoenzymes responsible for the metabolism of haloperidol. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and substrates or inhibitors of CYP3A4 or CYP2D6. Elevated haloperidol concentrations occurring through inhibition of CYP2D6 or CYP3A4 may increase the risk of adverse effects, including QT prolongation. Until more data are available, it is advisable to closely monitor for adverse events when these medications are co-administered.
Isoniazid, INH; Rifampin: (Major) Limited data suggest that rifampin, a potent CYP inducer, can increase the metabolism and/or reduce the bioavailability of haloperidol. In one small study (n=12), plasma levels of haloperidol were decreased by a mean of 70% and mean scores on the Brief Psychiatric Rating Scale (BPRS) were increased from baseline during concurrent use of rifampin. Discontinuation of rifampin has resulted in a mean 3.3-fold increase in haloperidol concentrations in some instances. Haloperidol dosage adjustments should be made as needed when rifampin is added or discontinued. Prolonged use of CYP inducers such as rifampin in patients receiving haloperidol has resulted in significant reductions in haloperidol plasma concentrations. (Moderate) Isoniazid, INH is a potent inhibitor of CYP3A4 and a mild inhibitor of CYP2D6, the isoenzymes responsible for the metabolism of haloperidol. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and substrates or inhibitors of CYP3A4 or CYP2D6. Elevated haloperidol concentrations occurring through inhibition of CYP2D6 or CYP3A4 may increase the risk of adverse effects, including QT prolongation. Until more data are available, it is advisable to closely monitor for adverse events when these medications are co-administered.
Isradipine: (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Itraconazole: (Major) Caution is advised when administering itraconazole with drugs that are known to prolong that QT interval and are metabolized by CYP3A4, such as haloperidol. Haloperidol is primarily metabolized by CYP2D6. However, in patients that are lacking in CYP2D6 enzyme activity (slow metabolizers), the CYP3A4 enzyme may play a larger role in haloperidol metabolism. Concurrent use of itraconazole (a potent inhibitor of CYP3A4) with haloperidol has resulted in increased serum haloperidol concentrations. Neurologic side effects and arrhythmias have been noted clinically in some patients because of impaired haloperidol elimination; however, QT prolongation has not been observed in single-dose studies. QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Itraconazole has also been associated with QT prolongation; coadministration with haloperidol may increase this risk. If these drugs must be used together, the haloperidol dose may need to be reduced and the patients should be monitored closely for adverse events. Of note, once itraconazole is discontinued, plasma concentrations decrease to almost undetectable concentrations within 7 to 14 days. The decline in plasma concentrations may be even more gradual in patients with hepatic cirrhosis or who are receiving concurrent CYP3A4 inhibitors.
Ivacaftor: (Moderate) Use caution when administering ivacaftor and haloperidol concurrently. Ivacaftor is an inhibitor of CYP3A and haloperidol is partially metabolized by CYP3A. Co-administration of ivacaftor with CYP3A substrates, such as haloperidol, can theoretically increase haloperidol exposure leading to increased or prolonged therapeutic effects and adverse events; however, the clinical impact of this has not yet been determined.
Ivosidenib: (Major) Avoid coadministration of ivosidenib with haloperidol due to an increased risk of QT prolongation. If concomitant use is unavoidable, monitor ECGs for QTc prolongation and monitor electrolytes; correct any electrolyte abnormalities as clinically appropriate. An interruption of therapy and dose reduction of ivosidenib may be necessary if QT prolongation occurs. Prolongation of the QTc interval and ventricular arrhythmias have been reported in patients treated with ivosidenib. QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation.
Kava Kava, Piper methysticum: (Major) Patients who are taking haloperidol should only use kava kava with prescriber approval and close monitoring. Additive sedation and CNS effects are possible, and inhibition of antipsychotic metabolism may occur. Additive sedation and CNS effects are possible. In addition, Haloperidol is a primary substrate of CYP2D6; at least 1 case report of potential pharmacokinetic interaction with kava kava has been published. Kava kava has been reported to inhibit many CYP isozymes, including CYP2D6.
Ketamine: (Major) Haloperidol can potentiate the actions of other CNS depressants such as general anesthetics. Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.
Ketoconazole: (Major) It is best to avoid ketoconazole with haloperidol. Haloperidol is primarily metabolized by CYP2D6. However, in patients that are lacking in CYP2D6 enzyme activity (slow metabolizers), the CYP3A4 enzyme plays a larger role in haloperidol metabolism. Concurrent use of ketoconazole (a potent inhibitor of CYP3A4) with haloperidol is likely to result in increased serum haloperidol concentrations; inhibition of haloperidol CYP3A4 metabolism is the suspected mechanism of the interaction. Increases in QTc have been observed during concurrent use of haloperidol with ketoconazole. Both ketoconazole and haloperidol have been associated with QT prolongation. QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. If use of these drugs is medically necessary, a reduced haloperidol dosage may be required.
Labetalol: (Moderate) Haloperidol should be used cautiously with labetalol due to the possibility of additive hypotension.
Lapatinib: (Major) Concurrent use of lapatinib and haloperidol should be avoided if possible. Lapatinib can prolong the QT interval. QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. According to the manufacturer of haloperidol, caution is advisable

when prescribing the drug concurrently with medications known to prolong the QT interval. In vitro, lapatinib is an inhibitor of CYP3A4. Elevated haloperidol concentrations occurring through inhibition of CYP3A4 may increase the risk of adverse effects, including QT prolongation. Monitor closely. Lapatinib can prolong the QT interval. Lapatinib should be administered with caution to patients who have or may develop prolongation of QTc such as patients taking medications that lead to QT prolongation such as haloperidol. Additionally, mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and inhibitors of CYP3A4 or CYP2D6. Therefore, it is advisable to closely monitor for adverse events when haloperidol is co-administered with inhibitors of CYP3A4 or CYP2D6 including lapatinib.
Lenvatinib: (Major) QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval. Drugs with a possible risk for QT prolongation and TdP that should be used cautiously and with close monitoring with haloperidol include lenvatinib. QT prolongation was reported in patients with radioactive iodine-refractory differentiated thyroid cancer (RAI-refractory DTC) in a double-blind, randomized, placebo-controlled clinical trial after receiving lenvatinib daily at the recommended dose; the QT/QTc interval was not prolonged, however, after a single 32 mg dose (1.3 times the recommended daily dose) in healthy subjects.
Letermovir: (Moderate) A clinically relevant increase in the plasma concentration of haloperidol may occur if given with letermovir. Haloperidol dose reductions may be needed in patients also receiving cyclosporine, because the magnitude of the interaction may be increased. Haloperidol is a CYP3A4 substrate. Letermovir is a moderate CYP3A4 inhibitor; however, when given with cyclosporine, the combined effect on CYP3A4 substrates is similar to a strong CYP3A4 inhibitor. In a drug interaction study, administration with another strong CYP3A4 inhibitor resulted in QT prolongation.
Leuprolide: (Major) When possible, avoid use of other drugs that may prolong the QT interval with haloperidol, due to additive risk factors. When use is necessary, close clinical monitoring may be needed. QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. Androgen deprivation therapy (e.g., leuprolide) prolongs the QT interval. Additionally, hjyperprolactinemia, which may be caused by antipsychotics, down-regulates the number of pituitary GnRH receptors and may interfere with the response to leuprolide therapy.
Leuprolide; Norethindrone: (Major) When possible, avoid use of other drugs that may prolong the QT interval with haloperidol, due to additive risk factors. When use is necessary, close clinical monitoring may be needed. QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. Androgen deprivation therapy (e.g., leuprolide) prolongs the QT interval. Additionally, hjyperprolactinemia, which may be caused by antipsychotics, down-regulates the number of pituitary GnRH receptors and may interfere with the response to leuprolide therapy.
Levocetirizine: (Moderate) Additive drowsiness may occur if cetirizine or levocetirizine is administered with other drugs that depress the CNS (e.g., haloperidol).
Levodopa: (Major) Antipsychotic agents may inhibit the clinical antiparkinsonian response to levodopa by blocking dopamine receptors in the brain. Haloperidol should be avoided during therapy for Parkinson's disease unless the benefit of the drug outweighs the risk of decreased therapeutic response to levodopa or other treatments.
Levofloxacin: (Major) Concurrent use of haloperidol and levofloxacin should be avoided due to an increased risk for QT prolongation and torsade de pointes (TdP). Levofloxacin has been associated with prolongation of the QT interval and infrequent cases of arrhythmia. Additionally, rare cases of TdP have been spontaneously reported during postmarketing surveillance in patients receiving levofloxacin. QT prolongation and TdP have also been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation.
Levomethadyl: (Severe) Levomethadyl is associated with an established risk of QT prolongation and/or torsades de pointes and is contraindicated in combination with other agents that may prolong the QT interval, including haloperidol.
Levorphanol: (Moderate) Concomitant use of levorphanol with other CNS depressants such as haloperidol can potentiate the effects of levorphanol on respiration, blood pressure, and alertness. Severe hypotension, respiratory depression, profound sedation, or coma may occur. Prior to concurrent use of levorphanol in patients taking a CNS depressant, assess the level of tolerance to CNS depression that has developed, the duration of use, and the patient's overall response to treatment. Consider the patient's use of alcohol or illicit drugs. When concomitant treatment with levorphanol with another CNS depressant is necessary, reduce the dose of 1 or both drugs. The initial dose of levorphanol should be reduced by approximately 50% or more when levorphanol is used with another drug that may depress respiration.
Lithium: (Major) Haloperidol and lithium are associated with QT prolongation. Coadministration may increase the risk of QT prolongation; therefore, haloperidol and lithium should be coadministered with caution and close monitoring. Some atypical antipsychotics are considered first-line adjunctive therapy to mood stabilizers such as lithium. However, it is advisable to monitor patients for neurotoxicity during co-administration. Neuroleptic malignant syndrome (NMS) has been observed occasionally during concurrent use of lithium and either atypical or conventional antipsychotics. Additive extrapyramidal effects have also been noted. Early case reports described an encephalopathic syndrome consisting of delirium, tremulousness, dyskinesia, seizures, leukocytosis, weakness, hyperpyrexia, confusion, extrapyramidal symptoms, elevations in laboratory values (e.g., liver function tests, blood urea nitrogen, fasting blood sugar) and, in some cases, irreversible brain damage, during use of lithium and conventional antipsychotics, particularly haloperidol. Subsequent rare reports of NMS or NMS-like reactions have been described during co-administration of lithium and atypical antipsychotics (e.g., risperidone, olanzapine, clozapine). Following resolution of NMS, there are isolated instances of re-emergence of symptoms following re-initiation of lithium as monotherapy. Lithium may be a risk factor for antipsychotic-induced NMS; however, this hypothesis has not been confirmed. In many reported cases, confounding factors have been present (e.g., previous history of NMS, high dose therapy). The ability of antipsychotics alone to precipitate NMS and the rarity of the condition further complicate assessment of lithium as a risk factor.
Lofexidine: (Major) Monitor ECG for QT prolongation during concurrent use of lofexidine and haloperidol. Lofexidine may prolong the QT interval, torsade de pointes (TdP) has been reported during postmarketing use. Haloperidol is associated with an established risk of QT prolongation and TdP. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation.
Lomefloxacin: (Major) These drugs should be used together with caution since there may be an increased risk for QT prolongation. Rare cases of torsade de pointes (TdP) have been spontaneously reported during postmarketing surveillance in patients receiving quinolones, including lomefloxacin. QT prolongation and TdP have been observed during haloperidol treatment. Excessive haloperidol doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation.
Long-acting beta-agonists: (Moderate) QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval. Beta-agonists may be associated with adverse cardiovascular effects including QT interval prolongation, usually at higher doses and/or when associated with hypokalemia. This risk may be more clinically significant with long-acting beta-agonists (i.e., formoterol, arformoterol, indacaterol, olodaterol, salmeterol, fluticasone; vilanterol, umeclidinium; vilanterol) than with short-acting beta-agonists. Beta-agonists should be administered with caution to patients being treated with drugs known to prolong the QT interval because the action of beta-agonists on the cardiovascular system may be potentiated.
Loop diuretics: (Major) QT prolongation has been observed during haloperidol treatment. Use of haloperidol and medications known to cause electrolyte imbalance may increase the risk of QT prolongation. Therefore, caution is advisable during concurrent use of haloperidol and loop diuretics. In general, haloperidol should also be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Loperamide: (Major) Loperamide should be used cautiously and with close monitoring with haloperidol. At high doses, loperamide has been associated with serious cardiac toxicities, including syncope, ventricular tachycardia, QT prolongation, torsade de pointes (TdP), and cardiac arrest. QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval. In addition, the plasma concentrations of loperamide, a CYP2D6 substrate, may be increased when administered concurrently with haloperidol, a CYP2D6 inhibitor, further increasing the risk of toxicity. If these drugs are used together, monitor for cardiac toxicities (i.e., syncope, ventricular tachycardia, QT prolongation, TdP, cardiac arrest) and other loperamide-associated adverse reactions, such as CNS effects.

Loperamide; Simethicone: (Major) Loperamide should be used cautiously and with close monitoring with haloperidol. At high doses, loperamide has been associated with serious cardiac toxicities, including syncope, ventricular tachycardia, QT prolongation, torsade de pointes (TdP), and cardiac arrest. QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval. In addition, the plasma concentrations of loperamide, a CYP2D6 substrate, may be increased when administered concurrently with haloperidol, a CYP2D6 inhibitor, further increasing the risk of toxicity. If these drugs are used together, monitor for cardiac toxicities (i.e., syncope, ventricular tachycardia, QT prolongation, TdP, cardiac arrest) and other loperamide-associated adverse reactions, such as CNS effects.
Lopinavir; Ritonavir: (Major) QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval, such as lopinavir. In addition, haloperidol is a substrate for CYP3A4 and CYP2D6. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and inhibitors of CYP3A4 or CYP2D6. Therefore, it is advisable to closely monitor for adverse events when haloperidol is co-administered with drugs that inhibit CYP3A4 and CYP2D6 and prolong the QT interval, such as lopinavir; ritonavir. (Major) Ritonavir is an inhibitor of CYP2D6 and CYP3A4, the isoenzymes responsible for the metabolism of haloperidol. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and inhibitors of CYP3A4 or CYP2D6. Elevated haloperidol concentrations occurring through inhibition of CYP2D6 or CYP3A4 may increase the risk of adverse effects, including QT prolongation. In addition, ritonavir also is associated with QT prolongation; concomitant use increases the risk of QT prolongation. Until more data are available, it is advisable to closely monitor for adverse events when these medications are co-administered.
Loratadine; Pseudoephedrine: (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol directly counteract the effects of pseudoephedrine and can counter the desired pharmacologic effect. They also can be used to treat excessive pseudoephedrine-induced hypertension.
Lorazepam: (Moderate) Haloperidol can potentiate the actions of other CNS depressants, such as benzodiazepines, Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.
Losartan: (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Loxapine: (Major) Caution is advisable during concurrent use of loxapine and other antipsychotics. Loxapine use has been associated with adverse events such as drowsiness, dizziness, orthostatic hypotension, anticholinergic effects, extrapyramidal symptoms, neuroleptic malignant syndrome, and seizures. These effects may be potentiated during concurrent use of loxapine and other antipsychotics. The likelihood of these pharmacodynamic interactions varies based upon the individual properties of the co-administered antipsychotic agent. Although the incidence of tardive dyskinesia from combination antipsychotic therapy has not been established and data are very limited, the risk appears to be increased during use of a conventional and atypical antipsychotic versus use of a conventional antipsychotic alone.
Lumacaftor; Ivacaftor: (Moderate) Lumacaftor; ivacaftor may decrease the systemic exposure and therapeutic efficacy of haloperidol with prolonged (1 to 2 weeks) coadministration. Carefully monitor clinical status when lumacaftor; ivacaftor is administered or discontinued in haloperidol-treated patients. Haloperidol may require dosage adjustment to achieve the desired clinical response. If lumacaftor; ivacaftor is subsequently discontinued, it may be necessary to reduce the haloperidol dosage. Haloperidol is a CYP3A substrate. Lumacaftor is a strong CYP3A inducer. Coadministration of haloperidol and rifampin, another strong CYP3A inducer, resulted in a 70% decrease in haloperidol plasma concentrations in 12 schizophrenic patients; correspondingly, Brief Psychiatric Rating Scale scores increased from baseline. In 5 other schizophrenic patients also treated with haloperidol and rifampin, antibiotic discontinuation resulted in a 3.3-fold increase in haloperidol concentrations. (Moderate) Use caution when administering ivacaftor and haloperidol concurrently. Ivacaftor is an inhibitor of CYP3A and haloperidol is partially metabolized by CYP3A. Co-administration of ivacaftor with CYP3A substrates, such as haloperidol, can theoretically increase haloperidol exposure leading to increased or prolonged therapeutic effects and adverse events; however, the clinical impact of this has not yet been determined.
Lumacaftor; Ivacaftor: (Moderate) Lumacaftor; ivacaftor may decrease the systemic exposure and therapeutic efficacy of haloperidol with prolonged (1 to 2 weeks) coadministration. Carefully monitor clinical status when lumacaftor; ivacaftor is administered or discontinued in haloperidol-treated patients. Haloperidol may require dosage adjustment to achieve the desired clinical response. If lumacaftor; ivacaftor is subsequently discontinued, it may be necessary to reduce the haloperidol dosage. Haloperidol is a CYP3A substrate. Lumacaftor is a strong CYP3A inducer. Coadministration of haloperidol and rifampin, another strong CYP3A inducer, resulted in a 70% decrease in haloperidol plasma concentrations in 12 schizophrenic patients; correspondingly, Brief Psychiatric Rating Scale scores increased from baseline. In 5 other schizophrenic patients also treated with haloperidol and rifampin, antibiotic discontinuation resulted in a 3.3-fold increase in haloperidol concentrations.
Lurasidone: (Major) Similar to other antipsychotics, lurasidone administration has been associated with drowsiness, dizziness, orthostatic hypotension, extrapyramidal symptoms, neuroleptic malignant syndrome, and seizures. The risk of these adverse effects may be increased during concurrent use of lurasidone with other antipsychotics. The likelihood of these pharmacodynamic interactions varies based upon the individual properties of the co-administered antipsychotic agent (see separate drug monographs). Although the incidence of tardive dyskinesia from combination antipsychotic therapy has not been established and data are very limited, the risk appears to be increased during use of a conventional and atypical antipsychotic versus use of a conventional antipsychotic alone.
Macimorelin: (Major) Avoid concurrent administration of macimorelin with drugs that prolong the QT interval, such as haloperidol. Use of these drugs together may increase the risk of developing torsade de pointes-type ventricular tachycardia. Sufficient washout time of drugs that are known to prolong the QT interval prior to administration of macimorelin is recommended. Treatment with macimorelin has been associated with an increase in the corrected QT (QTc) interval. QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation.
Maprotiline: (Major) Haloperidol can potentiate the actions of other CNS depressants such as cyclic antidepressants. Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects. Limited data suggest that haloperidol may inhibit the metabolism of some tricyclic antidepressants, however, the clinical significance of this interaction and the effect on maprotiline is uncertain. Haloperidol is an inhibitor of hepatic CYP2D6, and coadministration with maprotiline (CYP2D6 substrate) may lead to elevated maprotiline serum concentrations, potentiating toxicity. Haloperidol has also been associated with a possible risk for QT prolongation and/or torsades de pointes, particularly when excessive doses are used or in overdose. Haloperidol should be used cautiously with other agents that may have this effect (e.g., maprotiline).
Meclizine: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur.
Mefloquine: (Major) Mefloquine alone has not been reported to cause QT prolongation. However, due to the lack of clinical data, mefloquine should be used with extreme caution in patients receiving drugs that prolong the QT interval, such as haloperidol.
Meperidine: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as opiate agonists. Dose reduction of one or both drugs is necessary.
Meperidine; Promethazine: (Major) Promethazine, a phenothiazine, is associated with a possible risk for QT prolongation. Due to the risk of additive QT prolongation and potential for serious arrhythmias, promethazine should be used with caution in patients receiving haloperidol. In addition, co-administration of promethazine with haloperidol may increase the risk of adverse effects such as drowsiness, dizziness, orthostatic hypotension, anticholinergic effects, extrapyramidal symptoms, neuroleptic malignant syndrome, or seizures. Although the incidence of tardive dyskinesia from these combinations has not been established and data are very limited, the risk may be increased during combined use versus use of an antipsychotic alone. if use together is not avoidable, monitor closely. (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as opiate agonists. Dose reduction of one or both drugs is necessary.
Mephobarbital: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as barbiturates. Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.
Meprobamate: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as anxiolytics, sedatives, and hypnotics, and they should be used cautiously in combination.
Mesoridazine: (Severe) Due to the risk for QT prolongation and potential for serious arrhythmias, as well as duplicative antipsychotic effects, the

concurrent use of haloperidol with mesoridazine is contraindicated. QT prolongation and torsade de pointes have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. Mesoridazine is associated with an established risk for QT prolongation and torsade de pointes (TdP). Coadministration may increase the risk of adverse effects such as drowsiness, dizziness, orthostatic hypotension, anticholinergic effects, extrapyramidal symptoms, neuroleptic malignant syndrome, or seizures. Although the incidence of tardive dyskinesia from combination antipsychotic therapy has not been established and data are very limited, the risk appears to be increased during use of a conventional and atypical antipsychotic versus use of a conventional antipsychotic alone.

Methadone: (Major) The need to coadminister methadone with drugs known to prolong the QT interval should be done with extreme caution and a careful assessment of treatment risks versus benefits. Methadone is considered to be associated with an increased risk for QT prolongation and torsades de pointes (TdP), especially at higher doses (> 200 mg/day but averaging approximately 400 mg/day in adult patients). In addition, methadone is a substrate for CYP3A4, CYP2D6, and P-glycoprotein (P-gp). Concurrent use of methadone with inhibitors of these enzymes may result in increased serum concentrations of methadone. Drugs with a possible risk for QT prolongation and TdP that inhibit CYP2D6 include haloperidol. Concomitant use of methadone with another CNS depressant, such as haloperidol, can also lead to additive respiratory depression, hypotension, profound sedation, or coma. Prior to concurrent use of methadone in patients taking a CNS depressant, assess the level of tolerance to CNS depression that has developed, the duration of use, and the patient's overall response to treatment. Consider the patient's use of alcohol or illicit drugs. Methadone should be used with caution and in reduced dosages if used concurrently with a CNS depressant; in opioid-naive adults, use an initial methadone dose of 2.5 mg every 12 hours. Also consider a using a lower dose of the CNS depressant. Monitor patients for sedation and respiratory depression.

Methazolamide: (Major) QT prolongation has been observed during haloperidol treatment. Use of haloperidol and medications known to cause electrolyte imbalance may increase the risk of QT prolongation. Therefore, caution is advisable during concurrent use of haloperidol and methazolamide.

Methenamine; Sodium Acid Phosphate; Methylene Blue; Hyoscyamine: (Moderate) Additive adverse effects resulting from cholinergic blockade may occur when hyoscyamine is administered concomitantly with haloperidol.

Methohexital: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as barbiturates. Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.

Methyclothiazide: (Major) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. The risk of QT prolongation may also be increased during use of haloperidol and medications known to cause electrolyte imbalance such as thiazide diuretics.

Methyldopa: (Moderate) Disturbances of orthostatic regulation (e.g., orthostatic hypotension, dizziness, fatigue) and additive sedation may occur in patients receiving concomitant clonidine and antipsychotics. Also, based on observations in patients in a state of alcoholic delirium, high intravenous doses of clonidine may increase the arrhythmogenic potential (QT prolongation, ventricular fibrillation) of high intravenous doses of haloperidol. A causal relationship and relevance for clonidine oral tablets have not been established.

Methylphenidate: (Moderate) Antipsychotics, such as haloperidol, and methylphenidate may interact pharmacodynamically to diminish the therapeutic effects of either agent through opposing effects on dopamine. Methylphenidate blocks central dopamine reuptake, which has the potential to exacerbate psychosis, and antipsychotics, which are central dopamine antagonists, may diminish the effectiveness of methylphenidate.

Metoclopramide: (Severe) Metoclopramide is a central dopamine antagonist and may cause extrapyramidal reactions (e.g., acute dystonic reactions, pseudo-parkinsonism, akathisia, tardive dyskinesia), and rarely, neuroleptic malignant syndrome. Metoclopramide is contraindicated with other drugs that are likely to cause extrapyramidal effects since the risk of these effects may be increased. Antipsychotics are associated with a well-established risk of extrapyramidal effects. High potency agents (e.g., haloperidol) generally cause acute extrapyramidal symptoms more commonly than low potency agents or atypical antipsychotics. Additionally, because both antipsychotics and metoclopramide can cause sedation, seizures, or increased prolactin levels, it is possible that the risk of these effects may be increased during concurrent use.

Metolazone: (Major) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. The risk of QT prolongation may also be increased during use of haloperidol and medications known to cause electrolyte imbalance such as thiazide diuretics.

Metoprolol: (Moderate) Monitor for increased metoprolol adverse reactions including bradycardia and hypotension during coadministration. A dosage reduction for metoprolol may be needed based on response. Concurrent use may increase metoprolol exposure. Metoprolol is a CYP2D6 substrate; haloperidol is a moderate CYP2D6 inhibitor. In the presence of another moderate CYP2D6 inhibitor, the AUC of metoprolol was increased by 3.29-fold with no effect on the cardiovascular response to metoprolol.

Metronidazole: (Major) Potential QT prolongation has been reported in limited case reports with metronidazole. Drugs with a possible risk for QT prolongation and TdP that should be used cautiously and with close monitoring with metronidazole include haloperidol.

Metyrapone: (Moderate) Metyrapone may cause dizziness and/or drowsiness. Other drugs that may also cause drowsiness, such as haloperidol, should be used with caution. Additive drowsiness and/or dizziness is possible.

Metyrosine: (Moderate) The extrapyramidal effects of haloperidol can be increased by concomitant administration of metyrosine.

Mexiletine: (Moderate) Mexiletine is significantly metabolized by CYP2D6 isoenzymes. CYP2D6 inhibitors, such as haloperidol, could theoretically impair mexiletine metabolism; the clinical significance of such interactions is unknown.

Midazolam: (Moderate) Haloperidol can potentiate the actions of other CNS depressants, such as benzodiazepines, Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.

Midostaurin: (Major) The concomitant use of midostaurin and haloperidol may lead to additive QT interval prolongation. If these drugs are used together, consider electrocardiogram monitoring. In clinical trials, QT prolongation has been reported in patients who received midostaurin as single-agent therapy or in combination with cytarabine and daunorubicin. QT prolongation and torsade de pointes have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation.

Mifepristone: (Major) Avoid use together if possible due to an additive risk for QT prolongation and elevated haloperidol concentrations, which may lead to drug-related adverse events. Consider alternatives to haloperidol if possible. If use together is necessary, some patients may require haloperidol dose reduction; closely monitor for adverse events. Mifepristone inhibits CYP3A4 and has been associated with QT prolongation. QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. Mild to moderate increases in haloperidol exposure have been reported during concurrent use with inhibitors of CYP3A4.

Mirabegron: (Moderate) Mirabegron is a substrate and a moderate inhibitor of CYP2D6. Exposure of drugs metabolized by CYP2D6 such as haloperidol may be increased when co-administered with mirabegron. Haloperidol is primarily metabolized by CYP2D6. In addition, in vitro data suggest that haloperidol has CYP2D6 inhibitory effects and has the potential to decrease the metabolism of CYP2D6 substrates such as mirabegron. Therefore, appropriate monitoring and dose adjustment may be necessary.

Mirtazapine: (Major) There may be an increased risk for QT prolongation and torsade de pointes (TdP) during concurrent use of mirtazapine and haloperidol. Coadminister with caution. QT prolongation and TdP have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. Cases of QT prolongation, TdP, ventricular tachycardia, and sudden death have been reported during postmarketing use of mirtazapine, primarily following overdose or in patients with other risk factors for QT prolongation, including concomitant use of other medications associated with QT prolongation.

Mitotane: (Major) Use caution if mitotane and haloperidol are used concomitantly, and monitor for decreased efficacy of haloperidol and a possible change in dosage requirements. Mitotane is a strong CYP3A4 inducer and haloperidol is a CYP3A4 substrate in vitro; coadministration may result in decreased plasma concentrations of haloperidol. Limited data suggest that rifampin, another potent CYP inducer, can increase the metabolism and/or reduce the bioavailability of haloperidol. In one small study (n=12), plasma levels of haloperidol were decreased by a mean of 70% and mean scores on the Brief Psychiatric Rating Scale (BPRS) were increased from baseline during concurrent use of rifampin; discontinuation of rifampin resulted in a mean 3.3-fold increase in haloperidol concentrations in some instances. In another study (n = 11), patients who received increasing doses of carbamazepine had decreasing haloperidol plasma concentrations in linear proportion to the increasing carbamazepine concentrations. Careful monitoring of clinical status is warranted when CYP3A enzyme inducing drugs are administered or discontinued in haloperidol-treated

patients. Additionally, mitotane can cause sedation, lethargy, vertigo, and other CNS adverse reactions; additive CNS effects may occur initially when mitotane is given concurrently with haloperidol.
Molindone: (Major) Close monitoring is advisable during concurrent use of molindone with other antipsychotics. Because molindone shares certain pharmacological properties with other antipsychotics, additive cardiac effects (e.g., hypotension), CNS effects (e.g., drowsiness), or anticholinergic effects (e.g., constipation, xerostomia) may occur. Clinicians should note that antimuscarinic effects might be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation.
Morphine: (Moderate) Concomitant use of morphine with other CNS depressants can potentiate the effects of morphine on respiration, blood pressure, and alertness; examples of other CNS depressants include haloperidol. Prior to concurrent use of morphine in patients taking a CNS depressant, assess the level of tolerance to CNS depression that has developed, the duration of use, and the patient's overall response to treatment. Consider the patient's use of alcohol or illicit drugs. If a CNS depressant is used concurrently with morphine, a reduced dosage of morphine and/or the CNS depressant is recommended; for extended-release products, start with the lowest possible dose of morphine (i.e., 15 mg PO every 12 hours, extended-release tablets; 30 mg or less PO every 24 hours; extended-release capsules). Monitor patients for sedation and respiratory depression.
Morphine; Naltrexone: (Moderate) Concomitant use of morphine with other CNS depressants can potentiate the effects of morphine on respiration, blood pressure, and alertness; examples of other CNS depressants include haloperidol. Prior to concurrent use of morphine in patients taking a CNS depressant, assess the level of tolerance to CNS depression that has developed, the duration of use, and the patient's overall response to treatment. Consider the patient's use of alcohol or illicit drugs. If a CNS depressant is used concurrently with morphine, a reduced dosage of morphine and/or the CNS depressant is recommended; for extended-release products, start with the lowest possible dose of morphine (i.e., 15 mg PO every 12 hours, extended-release tablets; 30 mg or less PO every 24 hours; extended-release capsules). Monitor patients for sedation and respiratory depression.
Moxifloxacin: (Major) Concurrent use of haloperidol and moxifloxacin should be avoided due to an increased risk for QT prolongation and torsade de pointes (TdP). Moxifloxacin has been associated with prolongation of the QT interval. Additionally, post-marketing surveillance has identified very rare cases of ventricular arrhythmias including TdP, usually in patients with severe underlying proarrhythmic conditions. The likelihood of QT prolongation may increase with increasing concentrations of moxifloxacin, therefore the recommended dose or infusion rate should not be exceeded. QT prolongation and TdP have also been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation.
Nabilone: (Moderate) Concomitant use of nabilone with other CNS depressants can potentiate the effects of nabilone on respiratory depression.
Nadolol: (Moderate) Haloperidol should be used cautiously with nadolol due to the possibility of additive hypotension.
Nafarelin: (Moderate) Antipsychotics may cause hyperprolactinemia and should not be administered concomitantly with nafarelin since hyperprolactinemia down-regulates the number of pituitary GnRH receptors.
Nalbuphine: (Moderate) Concomitant use of nalbuphine with other CNS depressants, such as haloperidol, can potentiate the effects of nalbuphine on respiratory depression, CNS depression, and sedation.
Naproxen; Pseudoephedrine: (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol directly counteract the effects of pseudoephedrine and can counter the desired pharmacologic effect. They also can be used to treat excessive pseudoephedrine-induced hypertension.
Nebivolol: (Moderate) Monitor for increased toxicity as well as increased therapeutic effect of nebivolol if coadministered with haloperidol. Nebivolol is metabolized by CYP2D6. Although data are lacking, significant CYP2D6 inhibitors, such as haloperidol, could potentially increase nebivolol plasma concentrations via CYP2D6 inhibition; the clinical significance of this potential interaction is unknown, but an increase in adverse effects is possible.
Nebivolol; Valsartan: (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. (Moderate) Monitor for increased toxicity as well as increased therapeutic effect of nebivolol if coadministered with haloperidol. Nebivolol is metabolized by CYP2D6. Although data are lacking, significant CYP2D6 inhibitors, such as haloperidol, could potentially increase nebivolol plasma concentrations via CYP2D6 inhibition; the clinical significance of this potential interaction is unknown, but an increase in adverse effects is possible.
Nefazodone: (Moderate) Nefazodone is an inhibitor of CYP3A4, one of the isoenzymes responsible for the metabolism of haloperidol. In one study, concurrent use of nefazodone and haloperidol resulted in a 36%, 13%, and 37% increase in mean AUC, highest concentration, and 12-h concentration values for haloperidol, respectively; however, only the increase in AUC was statistically significant. Elevated haloperidol concentrations occurring through inhibition of CYP3A4 may increase the risk of adverse effects, including QT prolongation or additive CNS effects. A lower doses of haloperidol may be required in some patients receiving this combination.
Nelfinavir: (Moderate) Nelfinavir is a substrate and inhibitor of CYP3A4, one of the isoenzymes responsible for the metabolism of haloperidol. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and substrates or inhibitors of CYP3A4. Until more data are available, it is advisable to closely monitor for adverse events when these medications are co-administered.
Nevirapine: (Major) Coadministration of haloperidol and nevirapine may result in a significant reduction in haloperidol serum concentrations. Carefully monitor the patient's response to haloperidol if nevirapine is administered or discontinued. Adjust the haloperidol dose if necessary. Haloperidol is a CYP3A4 substrate and nevirapine is a CYP3A4 inducer. When coadministered with other CYP3A4 inducers, haloperidol concentrations were decreased.
Nicardipine: (Major) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. In addition, nicardipine is an inhibitor of CYP2D6 and CYP3A4, the isoenzymes responsible for the metabolism of haloperidol. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and substrates or inhibitors of CYP3A4 or CYP2D6. Elevated haloperidol concentrations occurring through inhibition of cytochrome P450 pathways may increase the risk of adverse effects, including QT prolongation. Until more data are available, it is advisable to closely monitor for adverse events when these medications are co-administered.
Nifedipine: (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Nilotinib: (Major) Avoid the concomitant use of nilotinib with other agents that prolong the QT interval, such as haloperidol. Nilotinib is a CYP3A4 and CYP2D6 inhibitor and haloperidol is a substrate of CYP3A4 and CYP2D6; administering these drugs together may result in increased haloperidol levels. If the use of haloperidol is necessary, hold nilotinib therapy. If these drugs are used together, consider a haloperidol dose reduction and monitor patients for toxicity (e.g., QT interval prolongation).
Nisoldipine: (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Non-Ionic Contrast Media: (Major) Haloperidol lowers the seizure threshold and should be discontinued at least 48 hours before myelography and should not be resumed for at least 24 hours postprocedure.
Norfloxacin: (Major) Due to an increased risk for QT prolongation and torsade de pointes (TdP), caution is advised when administering haloperidol with norfloxacin. QT prolongation and TdP have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. Quinolones have also been associated with QT prolongation and TdP. For norfloxacin specifically, extremely rare cases of TdP were reported during post-marketing surveillance. These reports generally involved patients with concurrent medical conditions or concomitant medications that may have been contributory.
Octreotide: (Major) Arrhythmias, sinus bradycardia, and conduction disturbances have occurred during octreotide therapy, warranting more cautious monitoring during octreotide administration in higher risk patients with cardiac disease. Although QT prolongation has been reported rarely with octreotide, no causal relationship has been established relative to the development of torsades de pointes (TdP). Since bradycardia is a risk factor for development of TdP, the potential occurrence of bradycardia during octreotide administration could theoretically increase the risk of TdP in patients receiving drugs which prolong the QT interval. Until further data are available, it is suggested to use octreotide cautiously in patients receiving drugs which prolong the QT interval. Drugs which have been established to have a causal association with QT prolongation and TdP include haloperidol.
Ofloxacin: (Major) QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in

the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval, including ofloxacin.
Olanzapine: (Major) QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval, including olanzapine. Coadministration may increase the risk of adverse effects such as drowsiness, dizziness, orthostatic hypotension, anticholinergic effects, extrapyramidal symptoms, neuroleptic malignant syndrome, or seizures. The likelihood of these pharmacodynamic interactions varies based upon the individual properties of the co-administered antipsychotic agent. Although the incidence of tardive dyskinesia from combination antipsychotic therapy has not been established and data are very limited, the risk appears to be increased during use of a conventional and atypical antipsychotic versus use of a conventional antipsychotic alone.
Olmesartan: (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Ombitasvir; Paritaprevir; Ritonavir: (Major) Ritonavir is an inhibitor of CYP2D6 and CYP3A4, the isoenzymes responsible for the metabolism of haloperidol. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and inhibitors of CYP3A4 or CYP2D6. Elevated haloperidol concentrations occurring through inhibition of CYP2D6 or CYP3A4 may increase the risk of adverse effects, including QT prolongation. In addition, ritonavir also is associated with QT prolongation; concomitant use increases the risk of QT prolongation. Until more data are available, it is advisable to closely monitor for adverse events when these medications are co-administered.
Ondansetron: (Major) If ondansetron and haloperidol must be coadministered, ECG monitoring is recommended. Ondansetron has been associated with a dose-related increase in the QT interval and postmarketing reports of torsade de pointes (TdP). QT prolongation and TdP have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation.
Oritavancin: (Moderate) Haloperidol is metabolized by CYP3A4 and CYP2D6; oritavancin is a weak CYP3A4 and CYP2D6 inducer. Plasma concentrations and efficacy of haloperidol may be reduced if these drugs are administered concurrently.
Orphenadrine: (Moderate) Orphenadrine has mild anticholinergic activity. Concomitant use of orphenadrine and haloperidol may worsen schizophrenic symptoms. Tardive dyskinesia may also develop.
Osimertinib: (Major) Avoid coadministration of haloperidol with osimertinib if possible due to the risk of QT prolongation and torsade de pointes (TdP). If concomitant use is unavoidable, periodically monitor ECGs for QT prolongation and monitor electrolytes; an interruption of osimertinib therapy with dose reduction or discontinuation of therapy may be necessary if QT prolongation occurs. Concentration-dependent QTc prolongation occurred during clinical trials of osimertinib. QT prolongation and TdP have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation.
Oxaliplatin: (Major) Monitor electrolytes and ECGs for QT prolongation if coadministration of haloperidol with oxaliplatin is necessary; correct electrolyte abnormalities prior to administration of oxaliplatin. QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. QT prolongation and ventricular arrhythmias including fatal torsade de pointes have also been reported with oxaliplatin use in postmarketing experience.
Oxazepam: (Moderate) Haloperidol can potentiate the actions of other CNS depressants, such as benzodiazepines, Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.
Oxcarbazepine: (Major) Significant reductions in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and CYP3A4 enzyme-inducing drugs such as carbamazepine. Oxcarbazepine is an inducer of CYP3A4. In addition, decreased anticonvulsant efficacy is a possibility when an antipsychotic agent such as haloperidol is administered to patients receiving oxcarbazepine for a seizure disorder, because antipsychotics may lower the seizure threshold. Haloperidol dosage adjustments should be made as needed when oxcarbazepine is added or discontinued.
Oxycodone: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as opiate agonists. Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.
Oxymorphone: (Moderate) Concomitant use of oxymorphone with other CNS depressants may produce additive CNS depressant effects. Hypotension, profound sedation, coma, respiratory depression, or death may occur; examples of other CNS depressants include haloperidol. Prior to concurrent use of oxymorphone in patients taking a CNS depressant, assess the level of tolerance to CNS depression that has developed, the duration of use, and the patient's overall response to treatment. Consider the patient's use of alcohol or illicit drugs. If a CNS depressant is used concurrently with oxymorphone, a reduced dosage of oxymorphone (1/3 to 1/2 of the usual dose) and/or the CNS depressant is recommended. If the extended-release oxymorphone tablets are used concurrently with a CNS depressant, it is recommended to use an initial dosage of 5 mg PO every 12 hours. Monitor for sedation or respiratory depression.
Palbociclib: (Moderate) Monitor for an increase in haloperidol-related adverse reactions if coadministration with palbociclib is necessary. Haloperidol is a CYP3A4 substrate and palbociclib is a weak, time-dependent CYP3A4 inhibitor. In clinical trials, mild to moderately increased haloperidol concentrations have been reported when haloperidol was given concomitantly with CYP3A4 inhibitors.
Paliperidone: (Major) Paliperidone has been associated with QT prolongation. According to the manufacturer of paliperidone, the drug should be avoided in combination with other agents also known to have this effect. Other antipsychotics associated with a possible risk for QT prolongation and TdP based on varying levels of documentation include haloperidol. QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation.
Panobinostat: (Major) The co-administration of panobinostat with haloperidol is not recommended; QT prolongation has been reported with both agents. If concomitant use cannot be avoided, closely monitor patients for signs and symptoms of haloperidol toxicity, including QT prolongation and cardiac arrhythmias. Panobinostat is a CYP2D6 inhibitor and haloperidol is a CYP2D6 substrate. When a single-dose of a CYP2D6-sensitive substrate was administered after 3 doses of panobinostat (20 mg given on days 3, 5, and 8), the CYP2D6 substrate Cmax increased by 20% to 200% and the AUC value increased by 20% to 130% in 14 patients with advanced cancer; exposure was highly variable (coefficient of variance > 150%).
Paroxetine: (Major) Haloperidol is metabolized by CYP2D6 and CYP3A4 and concurrent use with inhibitors of these isoenzymes may result in elevated haloperidol plasma concentrations and adverse effects including extrapyramidal symptoms or QT prolongation. Paroxetine is a potent CYP2D6 inhibitor. Because symptoms consistent with elevated haloperidol levels have been observed during co-administration of SSRIs and haloperidol, patients receiving these combinations should be monitored for adverse effects such as dizziness, sedation, impaired psychomotor performance, extrapyramidal symptoms, and adverse cardiac effects.
Pasireotide: (Major) QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval, such as pasireotide.
Pazopanib: (Major) Coadministration of pazopanib and other drugs that prolong the QT interval is not advised; pazopanib has been reported to prolong the QT interval. QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. If pazopanib and haloperidol must be continued, closely monitor the patient for QT interval prolongation. In addition, pazopanib is a weak inhibitor of CYP3A4. Coadministration of pazopanib and haloperidol, a CYP3A4 substrate, may cause an increase in systemic concentrations of haloperidol. Use caution when concurrent administration of haloperidol and pazopanib is necessary.
Peginterferon Alfa-2b: (Moderate) Monitor for adverse effects associated with increased exposure to haloperidol if peginterferon alfa-2b is coadministered. Peginterferon alfa-2b is a CYP2D6 inhibitor, while haloperidol is a CYP2D6 substrate.
Pemoline: (Major) Concurrent use of antipsychotics, such as haloperidol, and pemoline should generally be avoided. Antipsychotics and stimulants may interact pharmacodynamically to diminish the therapeutic effects of either agent through opposing effects on dopamine. The pharmacology of pemoline is poorly understood, but the drug may block central dopamine reuptake, which has the potential to exacerbate psychosis, and antipsychotics, which are central dopamine antagonists, may diminish the effectiveness of pemoline.

Penbutolol: (Moderate) Haloperidol should be used cautiously with penbutolol due to the possibility of additive hypotension.
Pentamidine: (Major) QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval, including pentamidine.
Pentazocine: (Moderate) Concomitant use of pentazocine with other CNS depressants can potentiate respiratory depression, CNS depression, and sedation. Pentazocine should be used cautiously in any patient receiving these agents, which may include haloperidol.
Pentazocine; Naloxone: (Moderate) Concomitant use of pentazocine with other CNS depressants can potentiate respiratory depression, CNS depression, and sedation. Pentazocine should be used cautiously in any patient receiving these agents, which may include haloperidol.
Pentobarbital: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as barbiturates. Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.
Perampanel: (Moderate) Co-administration of perampanel with CNS depressants, including ethanol, may increase CNS depression. The combination of perampanel (particularly at high doses) with ethanol has led to decreased mental alertness and ability to perform complex tasks (such as driving), as well as increased levels of anger, confusion, and depression; similar reactions should be expected with concomitant use of other CNS depressants, such as haloperidol.
Pergolide: (Major) Agents with dopamine antagonist properties, including butyrophenones, may decrease the effectiveness of dopamine agonists. These agents can cause abrupt and severe worsening of Parkinson's disease symptoms and should be avoided, if possible, in patients treated with dopamine agonists.
Perindopril; Amlodipine: (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Perphenazine: (Major) Perphenazine, a phenothiazine, is associated with a possible risk for QT prolongation. Theoretically, perphenazine may increase the risk of QT prolongation if coadministered with drugs with a possible risk for QT prolongation, such as haloperidol. Co-administration of perphenazine with haloperidol may increase the risk of adverse effects such as drowsiness, dizziness, orthostatic hypotension, anticholinergic effects, extrapyramidal symptoms, neuroleptic malignant syndrome, or seizures. The likelihood of these pharmacodynamic interactions varies based upon the individual properties of the co-administered antipsychotic agent. Although the incidence of tardive dyskinesia from combination antipsychotic therapy has not been established and data are very limited, the risk appears to be increased during use of a conventional and atypical antipsychotic versus use of a conventional antipsychotic alone.
Perphenazine; Amitriptyline: (Major) Perphenazine, a phenothiazine, is associated with a possible risk for QT prolongation. Theoretically, perphenazine may increase the risk of QT prolongation if coadministered with drugs with a possible risk for QT prolongation, such as haloperidol. Co-administration of perphenazine with haloperidol may increase the risk of adverse effects such as drowsiness, dizziness, orthostatic hypotension, anticholinergic effects, extrapyramidal symptoms, neuroleptic malignant syndrome, or seizures. The likelihood of these pharmacodynamic interactions varies based upon the individual properties of the co-administered antipsychotic agent. Although the incidence of tardive dyskinesia from combination antipsychotic therapy has not been established and data are very limited, the risk appears to be increased during use of a conventional and atypical antipsychotic versus use of a conventional antipsychotic alone.
Phenobarbital: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as barbiturates. Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.
Phenoxybenzamine: (Moderate) In general, haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Phentolamine: (Moderate) In general, haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Phenylephrine: (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol, directly counteract the effects of phenylephrine and can counter the desired pharmacologic effect. They also can be used to treat excessive phenylephrine-induced hypertension.
Phenylephrine; Promethazine: (Major) Promethazine, a phenothiazine, is associated with a possible risk for QT prolongation. Due to the risk of additive QT prolongation and potential for serious arrhythmias, promethazine should be used with caution in patients receiving haloperidol. In addition, co-administration of promethazine with haloperidol may increase the risk of adverse effects such as drowsiness, dizziness, orthostatic hypotension, anticholinergic effects, extrapyramidal symptoms, neuroleptic malignant syndrome, or seizures. Although the incidence of tardive dyskinesia from these combinations has not been established and data are very limited, the risk may be increased during combined use versus use of an antipsychotic alone. if use together is not avoidable, monitor closely. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol, directly counteract the effects of phenylephrine and can counter the desired pharmacologic effect. They also can be used to treat excessive phenylephrine-induced hypertension.
Pimavanserin: (Major) Pimavanserin may cause QT prolongation and should generally be avoided in patients receiving other medications known to prolong the QT interval, such as haloperidol. QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. Coadministration may increase the risk for QT prolongation.
Pimozide: (Severe) Haloperidol has a risk of QT prolongation and is contraindicated with pimozide. Concurrent use of pimozide with haloperidol may increase the risk of adverse effects such as drowsiness, sedation, dizziness, orthostatic hypotension, extrapyramidal symptoms, neuroleptic malignant syndrome, or seizures. The likelihood of these pharmacodynamic interactions varies based upon the individual properties of the co-administered antipsychotic agent. Although the incidence of tardive dyskinesia from combination antipsychotic therapy has not been established and data are very limited, the risk appears to be increased during use of a conventional and atypical antipsychotic versus use of a conventional antipsychotic alone. Haloperidol is an inhibitor of CYP2D6, one of the metabolic pathways of pimozide.
Pindolol: (Moderate) Haloperidol should be used cautiously with pindolol due to the possibility of additive hypotension.
Posaconazole: (Severe) The concurrent use of posaconazole and haloperidol is contraindicated due to the risk of life threatening arrhythmias such as torsade de pointes (TdP). Posaconazole is a potent inhibitor of CYP3A4, an isoenzyme responsible for the metabolism of haloperidol. These drugs used in combination may result in elevated haloperidol plasma concentrations, causing an increased risk for haloperidol-related adverse events, such as QT prolongation. Additionally, posaconazole has been associated with prolongation of the QT interval as well as rare cases of torsade de pointes; avoid use with other drugs that may prolong the QT interval and are metabolized through CYP3A4, such as haloperidol.
Potassium-sparing diuretics: (Moderate) In general, haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Pramipexole: (Major) Antipsychotic agents may inhibit the clinical antiparkinsonian response to levodopa, pergolide, pramipexole, or ropinirole therapy by blocking dopamine receptors in the brain. Haloperidol may also cause additive sedation with drugs like entacapone, pramipexole, ropinirole and tolcapone. In general, traditional antipsychotics are more likely to interfere with these therapies than newer, atypical antipsychotic agents. Haloperidol should be avoided during therapy for Parkinson's disease unless the benefit of the drug outweighs the risk of decreased therapeutic response to levodopa or other treatments.
Prazosin: (Moderate) In general, haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Prilocaine; Epinephrine: (Major) Use of epinephrine to treat droperidol or haloperidol -induced hypotension can result in a paradoxical lowering of blood pressure due to droperidol's alpha-blocking effects. Avoid using epinephrine concurrently with droperidol and haloperidol.
Primaquine: (Major) Due to the potential for QT interval prolongation with primaquine, caution is advised with other drugs that prolong the QT interval. Drugs with a possible risk for QT prolongation and TdP that should be used cautiously and with close monitoring with primaquine include haloperidol.
Primidone: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as barbiturates. Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.
Procainamide: (Major) Haloperidol should be used cautiously with procainamide. Procainamide administration is associated with QT prolongation and torsades de pointes (TdP). QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation.
Prochlorperazine: (Moderate) Prochlorperazine, a phenothiazine, is associated with a possible risk for QT prolongation. Theoretically,

prochlorperazine may increase the risk of QT prolongation if coadministered with drugs with a possible risk for QT prolongation, such as haloperidol. Co-administration of prochlorperazine with haloperidol may increase the risk of adverse effects such as drowsiness, dizziness, orthostatic hypotension, anticholinergic effects, extrapyramidal symptoms, neuroleptic malignant syndrome, or seizures. The likelihood of these pharmacodynamic interactions varies based upon the individual properties of the co-administered antipsychotic agent. Although the incidence of tardive dyskinesia from combination antipsychotic therapy has not been established and data are very limited, the risk appears to be increased during use of a conventional and atypical antipsychotic versus use of a conventional antipsychotic alone.
Promethazine: (Major) Promethazine, a phenothiazine, is associated with a possible risk for QT prolongation. Due to the risk of additive QT prolongation and potential for serious arrhythmias, promethazine should be used with caution in patients receiving haloperidol. In addition, co-administration of promethazine with haloperidol may increase the risk of adverse effects such as drowsiness, dizziness, orthostatic hypotension, anticholinergic effects, extrapyramidal symptoms, neuroleptic malignant syndrome, or seizures. Although the incidence of tardive dyskinesia from these combinations has not been established and data are very limited, the risk may be increased during combined use versus use of an antipsychotic alone. if use together is not avoidable, monitor closely.
Propafenone: (Major) Due to the potential for QT prolongation and torsade de pointes (TdP), caution is advised when administering propafenone with haloperidol. Propafenone is a Class IC antiarrhythmic which increases the QT interval largely due to prolongation of the QRS interval. QT prolongation and TdP have also been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. In addition, haloperidol is a substrate for CYP2D6 and propafenone is a CYP2D6 substrate/inhibitor. Mild to moderate increases in haloperidol plasma concentrations may occur during concurrent use.
Propofol: (Major) Haloperidol can potentiate the actions of other CNS depressants such as general anesthetics. Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.
Propoxyphene: (Moderate) Propoxyphene is a substrate and an inhibitor of CYP2D6. Increased serum concentrations of propoxyphene would be expected from concurrent use of a CYP2D6 inhibitor, such as haloperidol.
Propranolol: (Moderate) Haloperidol should be used cautiously with propranolol due to the possibility of additive hypotension and increased concentrations of propranolol. Propranolol is significantly metabolized by CYP2D6 isoenzymes. A case report of 3 severe hypotension episodes (2 requiring cardiopulmonary resuscitation) has been reported in one 48 year old woman when propranolol and haloperidol have been coadministered. Additive hypotensive effects and haloperidol-mediated CYP2D6 inhibition may have contributed to this interaction.
Pseudoephedrine: (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol directly counteract the effects of pseudoephedrine and can counter the desired pharmacologic effect. They also can be used to treat excessive pseudoephedrine-induced hypertension.
Quazepam: (Moderate) Concomitant administration of quazepam with CNS-depressant drugs, such as antipsychotics, can potentiate the CNS effects of either agent.
Quetiapine: (Major) Quetiapine may be associated with a significant prolongation of the QTc interval in rare instances. According to the manufacturer, use of quetiapine should be avoided in combination with drugs that have established causal association with QT prolongation and TdP (torsade de pointes), like haloperidol. Coadministration may increase the risk of adverse effects such as drowsiness, dizziness, orthostatic hypotension, anticholinergic effects, extrapyramidal symptoms, neuroleptic malignant syndrome, or seizures. The likelihood of these pharmacodynamic interactions varies based upon the individual properties of the co-administered antipsychotic agent. Although the incidence of tardive dyskinesia from combination antipsychotic therapy has not been established and data are very limited, the risk appears to be increased during use of a conventional and atypical antipsychotic versus use of a conventional antipsychotic alone.
Quinidine: (Severe) Quinidine should be considered contraindicated with haloperidol. QT prolongation and torsade de pointes (TdP) have been observed during both haloperidol and quinidine treatment. Excessive doses (particularly in the overdose setting) of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval; however, quinidine is contraindicated for use with drugs that are CYP2D6 substrates that prolong the QT interval. Pretreatment with quinidine caused peak haloperidol serum concentrations and haloperidol AUC to increase.
Quinine: (Major) Concurrent use of quinine and haloperidol should be avoided due to an increased risk for QT prolongation and torsade de pointes (TdP). Quinine has been associated with prolongation of the QT interval and rare cases of TdP. QT prolongation and TdP have also been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. Further, quinine is a substrate of CYP3A4 and an inhibitor of CYP2D6 and CYP3A4, the isoenzymes responsible for the metabolism of haloperidol. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and inhibitors of CYP3A4 or CYP2D6. Elevated haloperidol concentrations occurring through inhibition of CYP2D6 or CYP3A4 may increase the risk of adverse effects, including QT prolongation.
Ramelteon: (Moderate) An enhanced CNS depressant effect may occur when haloperidol is combined with other CNS depressants including sedating h1-blockers.
Ranolazine: (Major) It is prudent to avoid concurrent use of ranolazine and haloperidol if possible, and to evaluate the risks and benefits of alternative treatment options. Ranolazine is associated with dose- and plasma concentration-related increases in the QTc interval. The mean increase in QTc is about 6 milliseconds, measured at the tmax of the maximum dosage (1000 mg PO twice daily). However, in 5% of the population studied, increases in the QTc of at least 15 milliseconds have been reported. Although there are no studies examining the effects of ranolazine in patients receiving other QT prolonging drugs, coadministration of such drugs, including haloperidol, may result in additive QT prolongation. In addition, both ranolazine and haloperidol are CYP2D6 substrates and inhibitors. Theoretically, increased plasma concentrations of one or both drugs can occur during co-administration. Elevated haloperidol concentrations occurring through inhibition of CYP2D6 or CYP3A4 may increase the risk of adverse effects, including QT prolongation.
Rasagiline: (Moderate) Haloperidol may reduce the beneficial effects of rasagiline by blocking dopamine. Additive CNS effects are possible; advise against engaging in tasks requiring mental alertness until the effects of the drug combination are known to the patient. Monoamine oxidase type B inhibitors increase the availability of central dopamine. Haloperidol may induce pseudoparkinisonism (e.g., shuffling gait, tremor), thereby exacerbating Parkinson's disease symptoms. In addition, dopaminergic medications, including rasagiline, may cause a sudden onset of somnolence which sometimes has resulted in motor vehicle accidents. Patients may not perceive warning signs, such as excessive drowsiness, or they may report feeling alert immediately prior to the event. Haloperidol may be problematic in exacerbating sedation or hypotension.
Regadenoson: (Major) QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval. Drugs with a possible risk for QT prolongation and TdP that should be used cautiously with haloperidol include regadenoson.
Remifentanil: (Moderate) Concomitant use of remifentanil with other CNS depressants, such as haloperidol, can potentiate the effects of remifentanil on respiration, sedation, and hypotension. A dose reduction of one or both drugs may be warranted.
Reserpine: (Moderate) In general, haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Ribociclib: (Major) Avoid coadministration of ribociclib with haloperidol due to an increased risk for QT prolongation and torsade de pointes (TdP). Systemic exposure of haloperidol may also be increased resulting in an increase in haloperidol-related adverse reactions. Ribociclib has been shown to prolong the QT interval in a concentration-dependent manner. QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. Concomitant use may increase the risk for QT prolongation. Ribociclib is also a moderate CYP3A4 inhibitor and haloperidol is a CYP3A4 substrate.
Ribociclib; Letrozole: (Major) Avoid coadministration of ribociclib with haloperidol due to an increased risk for QT prolongation and torsade de pointes (TdP). Systemic exposure of haloperidol may also be increased resulting in an increase in haloperidol-related adverse reactions. Ribociclib has been shown to prolong the QT interval in a concentration-dependent manner. QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. Concomitant use may increase the risk for QT prolongation. Ribociclib is also a moderate CYP3A4 inhibitor and haloperidol is a CYP3A4 substrate.
Rifabutin: (Major) Significant reductions in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and

CYP3A4 enzyme-inducing drugs such as carbamazepine or rifampin. Rifabutin is an inducer and a substrate of CYP3A4. Haloperidol dosage adjustments should be made as needed when rifabutin is added or discontinued.
Rifampin: (Major) Limited data suggest that rifampin, a potent CYP inducer, can increase the metabolism and/or reduce the bioavailability of haloperidol. In one small study (n=12), plasma levels of haloperidol were decreased by a mean of 70% and mean scores on the Brief Psychiatric Rating Scale (BPRS) were increased from baseline during concurrent use of rifampin. Discontinuation of rifampin has resulted in a mean 3.3-fold increase in haloperidol concentrations in some instances. Haloperidol dosage adjustments should be made as needed when rifampin is added or discontinued. Prolonged use of CYP inducers such as rifampin in patients receiving haloperidol has resulted in significant reductions in haloperidol plasma concentrations.
Rifapentine: (Major) Rifapentine induces hepatic isoenzymes CYP3A4 and CYP2C8/9. Haloperidol is metabolized by CYP3A4 and CYP2C8/9 and may require dosage adjustments when administered concurrently with rifapentine.
Rilpivirine: (Major) Supratherapeutic doses of rilpivirine (75 to 300 mg/day) have caused QT prolongation; caution is advised when administering rilpivirine with other drugs that may prolong the QT or PR interval, such as haloperidol. QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation.
Risperidone: (Major) Caution is advisable when coadministering medications that have a possible risk of QT prolongation and torsade de pointes (TdP), including risperidone and haloperidol. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation than with routine oral dosing. Coadministration of haloperidol with risperidone may also increase the risk of adverse effects such as drowsiness, dizziness, orthostatic hypotension, anticholinergic effects, extrapyramidal symptoms, neuroleptic malignant syndrome, or seizures. Although the incidence of tardive dyskinesia from combination antipsychotic therapy has not been established and data are very limited, the risk appears to be increased during use of a conventional and atypical antipsychotic versus use of a conventional antipsychotic alone.
Ritonavir: (Major) Ritonavir is an inhibitor of CYP2D6 and CYP3A4, the isoenzymes responsible for the metabolism of haloperidol. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and inhibitors of CYP3A4 or CYP2D6. Elevated haloperidol concentrations occurring through inhibition of CYP2D6 or CYP3A4 may increase the risk of adverse effects, including QT prolongation. In addition, ritonavir also is associated with QT prolongation; concomitant use increases the risk of QT prolongation. Until more data are available, it is advisable to closely monitor for adverse events when these medications are co-administered.
Rolapitant: (Major) Monitor for haloperidol-related adverse effects, including QT prolongation, if coadministered with rolapitant. Increased exposure to haloperidol may occur. Haloperidol is a CYP2D6 substrate that is individually dose-titrated, and rolapitant is a moderate CYP2D6 inhibitor; the inhibitory effect of rolapitant is expected to persist beyond 28 days for an unknown duration. Exposure to another CYP2D6 substrate, following a single dose of rolapitant increased about 3-fold on Days 8 and Day 22. The inhibition of CYP2D6 persisted on Day 28 with a 2.3-fold increase in the CYP2D6 substrate concentrations, the last time point measured.
Romidepsin: (Major) Romidepsin has been reported to prolong the QT interval. If romidepsin must be coadministered with another drug that prolongs the QT interval, appropriate cardiovascular monitoring precautions should be considered, such as the monitoring of electrolytes and ECGs at baseline and periodically during treatment. Drugs with a possible risk for QT prolongation and TdP that should be used cautiously with romidepsin include haloperidol. QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation.
Ropinirole: (Major) Haloperidol may inhibit the clinical antiparkinsonian response to ropinirole therapy by blocking dopamine receptors in the brain. Haloperidol may also cause additive sedation with ropinirole. Haloperidol should be avoided during therapy for Parkinson's disease unless the benefit of the drug outweighs the risk of decreased therapeutic response to ropinirole.
Rotigotine: (Major) Avoid use together unless the benefits outweigh potential for reduced medication efficacy. Rotigotine is a dopamine-receptor agonist. Dopamine-receptor antagonists, including haloperidol, should be avoided concurrently because they may antagonize the effects of rotigotine. Monitor for an altered clinical response to drug therapy and for additive CNS effects if used together.
Rucaparib: (Moderate) Monitor for an increase in haloperidol-related adverse reactions if coadministration with rucaparib is necessary. Haloperidol is a CYP3A4 substrate and rucaparib is a weak CYP3A4 inhibitor. In clinical trials, mild to moderately increased haloperidol concentrations have been reported when haloperidol was given concomitantly with CYP3A4 inhibitors.
Sacubitril; Valsartan: (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Safinamide: (Moderate) Haloperidol may reduce the beneficial effects of safinamide by blocking dopamine. Additive CNS effects are possible; advise against engaging in tasks requiring mental alertness until the effects of the drug combination are known to the patient. Monoamine oxidase type B inhibitors increase the availability of central dopamine. Antipsychotics may induce pseudoparkinsonism (e.g., shuffling gait, tremor), thereby exacerbating Parkinson's disease symptoms. In addition, dopaminergic medications, including safinamide, may cause a sudden onset of somnolence which sometimes has resulted in motor vehicle accidents. Patients may not perceive warning signs, such as excessive drowsiness, or they may report feeling alert immediately prior to the event. Haloperidol may exacerbate sedation or hypotension.
Saquinavir: (Severe) Concurrent use of haloperidol and saquinavir boosted with ritonavir is contraindicated due to the risk for cardiac arrhythmias. QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Saquinavir boosted with ritonavir increases the QT interval in a dose-dependent fashion, which may increase the risk for serious arrhythmias such as TdP. In addition, saquinavir is an inhibitor of CYP3A4. Elevated haloperidol concentrations occurring through inhibition of CYP3A4 may increase the risk of adverse effects, including QT prolongation.
Secobarbital: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as barbiturates. Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.
Sertraline: (Major) There have been postmarketing reports of QT prolongation and torsade de pointes (TdP) during treatment with sertraline and the manufacturer of sertraline recommends avoiding concurrent use with drugs known to prolong the QTc interval. QT prolongation and TdP have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval. In addition, sertraline is a CYP2D6 inhibitor and pharmacokinetic interactions are possible with CYP2D6 substrates including haloperidol.
Sevoflurane: (Major) QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval. Drugs with a possible risk for QT prolongation and TdP that should be used cautiously and with close monitoring with haloperidol include halogenated anesthetics.
Short-acting beta-agonists: (Minor) QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval. Beta-agonists may be associated with adverse cardiovascular effects including QT interval prolongation, usually at higher doses and/or when associated with hypokalemia. This risk may be more clinically significant with long-acting beta-agonists (i.e., formoterol, arformoterol, indacaterol, olodaterol, salmeterol, fluticasone; vilanterol, umeclidinium; vilanterol) than with short-acting beta-agonists. Beta-agonists should be administered with caution to patients being treated with drugs known to prolong the QT interval because the action of beta-agonists on the cardiovascular system may be potentiated.
Sibutramine: (Major) Caution and close monitoring should be observed when administering sibutramine with drugs that are dopamine antagonists such as haloperidol. Monitor for CNS depression, changes in mood or behavior, and for other drug-related adverse reactions. Sibutramine has not been systematically evaluated in combination with antipsychotic medications. Sibutramine is a serotonin reuptake inhibitor that also inhibits norepinephrine and dopamine reuptake. Patients receiving these combinations should be monitored for the emergence of serotonin syndrome or neuroleptic malignant syndrome-like reactions.
Simeprevir: (Moderate) Simeprevir, a mild intestinal CYP3A4 inhibitor, may increase the side effects of haloperidol, which is a CYP3A4 substrate.

Monitor patients for adverse effects of haloperidol, such as QT prolongation and CNS effects.
Sodium Phenylbutyrate: (Moderate) Patients with urea cycle disorders being treated with sodium phenylbutyrate usually should not receive regular treatment with haloperidol. Haloperidol has been reported to increase plasma ammonia levels (hyperammonemia).
Sodium picosulfate; Magnesium oxide; Anhydrous citric acid: (Moderate) Use caution when prescribing sodium picosulfate; magnesium oxide; anhydrous citric acid in patients taking concomitant medications that are known to induce Antidiuretic Hormone Secretion (SIADH), such as antipsychotics, as these drugs may increase the risk of water retention and/or electrolyte imbalance.
Solifenacin: (Major) Solifenacin should be used cautiously and with close monitoring with haloperidol. Solifenacin has been associated with dose-dependent prolongation of the QT interval. Torsades de pointes (TdP) has been reported with post-marketing use, although causality was not determined. QT prolongation and TdP have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval.
Sorafenib: (Major) Sorafenib has been associated with QT prolongation. If sorafenib and another drug that prolongs the QT interval must be coadministered, ECG monitoring is recommended; closely monitor the patient for QT interval prolongation. Drugs with a possible risk for QT prolongation and TdP that should be used cautiously with sorafenib include haloperidol. QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation.
Sotalol: (Major) QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval. Sotalol administration is associated with QT prolongation and TdP. Proarrhythmic events should be anticipated after initiation of therapy and after each upward dosage adjustment.
Sparfloxacin: (Severe) Sparfloxacin is associated with an established risk for QT prolongation and torsade de pointes (TdP) and is contraindicated in patients receiving other drugs that can cause QT prolongation, including haloperidol. QT prolongation and TdP have also been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation.
Spironolactone: (Moderate) In general, haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
St. John's Wort, Hypericum perforatum: (Moderate) St. John's Wort appears to induce several isoenzymes of the hepatic cytochrome P450 enzyme system and could decrease the efficacy of some medications metabolized by these enzymes including haloperidol.
Streptogramins: (Moderate) Dalfopristin; quinupristin is an inhibitor of CYP3A4, one of the isoenzymes responsible for the metabolism of haloperidol. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and inhibitors of CYP3A4. Until more data are available, it is advisable to closely monitor for adverse events when these medications are co-administered.
Sufentanil: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as sufentanil. Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.
Sulfamethoxazole; Trimethoprim, SMX-TMP, Cotrimoxazole: (Major) QT prolongation resulting in ventricular tachycardia and torsade de pointes (TdP) have been reported during post-marketing use of sulfamethoxazole; trimethoprim. Drugs with a possible risk for QT prolongation and TdP that should be used cautiously and with close monitoring with sulfamethoxazole; trimethoprim include haloperidol.
Sunitinib: (Major) Monitor patients for QT prolongation if coadministration of haloperidol with sunitinib is necessary. Sunitinib can cause dose-dependent QT prolongation, which may increase the risk for ventricular arrhythmias, including torsades de points (TdP). Prolongation of the QT interval and TdP have been observed during haloperidol treatment; excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk.
Tacrine: (Major) Haloperidol excess has been associated with parkinsonian and dystonic reactions. It also appears that combining tacrine, a cholinergic agent, with haloperidol may predispose patients to these reactions.
Tacrolimus: (Major) Tacrolimus causes QT prolongation. Reducing the tacrolimus dose, close monitoring of tacrolimus whole blood concentrations, and monitoring for QT prolongation is recommended when coadministrating tacrolimus with other substrates and/or inhibitors of CYP3A4 that also have the potential to prolong the QT interval such as haloperidol. QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation.
Tamoxifen: (Major) Concomitant use of tamoxifen and haloperidol may cause an increased risk of QT prolongation and torsade de pointes (TdP); reduced tamoxifen efficacy and/or increased tamoxifen toxicity is also possible. If coadministration is unavoidable, monitor for altered tamoxifen efficacy, increased tamoxifen-related adverse effects, and evidence of QT prolongation. Tamoxifen has been reported to prolong the QT interval, usually in overdose or when used in high doses. Rare case reports of QT prolongation have also been described when tamoxifen is used at lower doses. QT prolongation and TdP have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. Haloperidol may reduce the conversion of tamoxifen to other potent active metabolites via inhibition of CYP2D6. In a clinical trial, there was a significantly higher rate of breast cancer recurrence in patients who had received a CYP2D6 inhibitor with tamoxifen. In another observational study, no clinically significant differences were observed with the addition of a CYP2D6 inhibitor to tamoxifen therapy; however, only 215 patients of 1,990 were administered a CYP2D6 inhibitor.
Tamsulosin: (Moderate) Use caution when administering tamsulosin with a moderate CYP2D6 inhibitor such as haloperidol. Tamsulosin is extensively metabolized by CYP2D6 hepatic enzymes. In clinical evaluation, concomitant treatment with a strong CYP2D6 inhibitor resulted in increases in tamsulosin exposure; interactions with moderate CYP2D6 inhibitors have not been evaluated. If concomitant use in necessary, monitor patient closely for increased side effects.
Tapentadol: (Moderate) Additive CNS depressive effects are expected if tapentadol is used in conjunction with other CNS depressants. Severe hypotension, profound sedation, coma, or respiratory depression may occur. Prior to concurrent use of tapentadol in patients taking a CNS depressant, assess the level of tolerance to CNS depression that has developed, the duration of use, and the patient's overall response to treatment. Consider the patient's use of alcohol or illicit drugs. If a CNS depressant is used concurrently with tapentadol, a reduced dosage of tapentadol and/or the CNS depressant is recommended. If the extended-release tapentadol tablets are used concurrently with a CNS depressant, it is recommended to use an initial tapentadol dose of 50 mg PO every 12 hours. Monitor patients for sedation and respiratory depression.
Telaprevir: (Moderate) Close clinical monitoring is advised when administering haloperidol with telaprevir due to an increased potential for haloperidol-related adverse events. If haloperidol dose adjustments are made, re-adjust the dose upon completion of telaprevir treatment. Although this interaction has not been studied, predictions about the interaction can be made based on the metabolic pathway of haloperidol. Haloperidol is partially metabolized by the hepatic isoenzyme CYP3A4; telaprevir inhibits this isoenzyme. Coadministration may result in elevated haloperidol plasma concentrations.
Telavancin: (Major) QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval, including telavancin.
Telithromycin: (Major) Telithromycin is associated with QT prolongation and torsades de pointes (TdP) and is a strong inhibitor of the CYP3A4 isoenzyme. Coadministration with other drugs that prolong the QT interval and are CYP3A4 substrates may result in increased concentrations of those drugs and an increased risk of adverse reactions, such as QT prolongation. Drugs with a possible risk of QT prolongation that are also CYP3A4 substrates that should be used cautiously with telithromycin include haloperidol.
Telmisartan: (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Telotristat Ethyl: (Moderate) Use caution if coadministration of telotristat ethyl and haloperidol is necessary, as the systemic exposure of haloperidol may be decreased resulting in reduced efficacy. If these drugs are used together, monitor patients for suboptimal efficacy of haloperidol; consider increasing the dose of haloperidol if necessary. Haloperidol is a CYP3A4 substrate. The mean Cmax and AUC of another sensitive CYP3A4 substrate was decreased by 25% and 48%, respectively, when coadministered with telotristat ethyl; the mechanism of this interaction

appears to be that telotristat ethyl increases the glucuronidation of the CYP3A4 substrate.
Temazepam: (Moderate) Caution should be exercised with simultaneous use of these agents. Haloperidol can potentiate the actions of other CNS depressants, such as the benzodiazepines. Complex sleep behaviors are more likely to occur when temazepam is taken with other CNS depressants. Warn patients of the possibility of drowsiness that may impair performance of potentially hazardous tasks such as driving an automobile or operating machinery.
Terazosin: (Moderate) In general, haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Terbinafine: (Moderate) In vitro studies have shown systemic terbinafine to inhibit hepatic isoenzyme CYP2D6, and thus may inhibit the clearance of drugs metabolized by this isoenzyme, such as haloperidol.
Tetrabenazine: (Major) Concurrent use of tetrabenazine and haloperidol should be avoided if possible. Tetrabenazine causes a small increase in the corrected QT interval (QTc). QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. The manufacturer of tetrabenazine recommends against concurrent use of tetrabenazine with other drugs known to prolong QTc. In addition, tetrabenazine is a selective, reversible, centrally-acting dopamine depleting drug and haloperidol is a central dopamine antagonist. The risk of adverse effects such as drowsiness, dizziness, orthostatic hypotension, neuroleptic malignant syndrome, or extrapyramidal symptoms may be increased.
Tezacaftor; Ivacaftor: (Moderate) Use caution when administering ivacaftor and haloperidol concurrently. Ivacaftor is an inhibitor of CYP3A and haloperidol is partially metabolized by CYP3A. Co-administration of ivacaftor with CYP3A substrates, such as haloperidol, can theoretically increase haloperidol exposure leading to increased or prolonged therapeutic effects and adverse events; however, the clinical impact of this has not yet been determined.
Thalidomide: (Major) Avoid the concomitant use of thalidomide with antipsychotics due to the potential for additive sedative effects.
Thiazide diuretics: (Major) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. The risk of QT prolongation may also be increased during use of haloperidol and medications known to cause electrolyte imbalance such as thiazide diuretics.
Thiopental: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as barbiturates. Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.
Thioridazine: (Severe) Due to the risk for QT prolongation and potential for serious arrhythmias, as well as duplicative antipsychotic effects, the concurrent use of haloperidol with thioridazine is contraindicated. QT prolongation and torsade de pointes have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. Thioridazine is associated with an established risk for QT prolongation and torsade de pointes (TdP). Coadministration may increase the risk of adverse effects such as drowsiness, dizziness, orthostatic hypotension, anticholinergic effects, extrapyramidal symptoms, neuroleptic malignant syndrome, or seizures. Although the incidence of tardive dyskinesia from combination antipsychotic therapy has not been established and data are very limited, the risk appears to be increased during use of a conventional and atypical antipsychotic versus use of a conventional antipsychotic alone.
Thiothixene: (Major) Caution is advisable during concurrent use of thiothixene and other antipsychotics. Thiothixene use has been associated with adverse events such as drowsiness, dizziness, orthostatic hypotension, anticholinergic effects, extrapyramidal symptoms, neuroleptic malignant syndrome, and seizures. These effects may be potentiated during concurrent use of loxapine and other antipsychotics. The likelihood of these pharmacodynamic interactions varies based upon the individual properties of the co-administered antipsychotic agent. Although the incidence of tardive dyskinesia from combination antipsychotic therapy has not been established and data are very limited, the risk appears to be increased during use of a conventional and atypical antipsychotic versus use of a conventional antipsychotic alone.
Timolol: (Moderate) Haloperidol should be used cautiously with timolol due to the possibility of additive hypotension.
Tipranavir: (Moderate) Tipranavir is a potent inhibitor of CYP2D6 and CYP3A4, the isoenzymes responsible for the metabolism of haloperidol. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and inhibitors of CYP3A4 or CYP2D6. Elevated haloperidol concentrations occurring through inhibition of CYP2D6 or CYP3A4 may increase the risk of adverse effects, including QT prolongation. Until more data are available, it is advisable to closely monitor for adverse events when these medications are co-administered.
Tizanidine: (Major) Haloperidol should be used cautiously and with close monitoring with tizanidine. Tizanidine administration may result in QT prolongation. QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval.
Tobacco: (Moderate) Tobacco smoke may accelerate the metabolism of haloperidol. Sudden cessation of tobacco smoking may result in a reduced clearance of this antipsychotic, despite the initiation of a nicotine replacement product. Monitor patients carefully when changes in smoking status occur.
Tolcapone: (Major) COMT inhibitors should be given cautiously with other agents that cause CNS depression, including haloperidol, due to the possibility of additive sedation.
Tolterodine: (Major) Due to the potential for QT prolongation and torsade de pointes (TdP), caution is advised when administering tolterodine with haloperidol. Tolterodine has been associated with dose-dependent prolongation of the QT interval, especially in poor CYP2D6 metabolizers. QT prolongation and TdP have also been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation.
Toremifene: (Major) Avoid coadministration of haloperidol with toremifene if possible due to the risk of additive QT prolongation. If concomitant use is unavoidable, closely monitor ECGs for QT prolongation and monitor electrolytes; correct hypokalemia or hypomagnesemia prior to administration of toremifene. Prolongation of the QT interval and torsade de pointes (TdP) have been observed during haloperidol treatment; excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk. Toremifene has also been shown to prolong the QTc interval in a dose- and concentration-related manner.
Torsemide: (Major) QT prolongation has been observed during haloperidol treatment. Use of haloperidol and medications known to cause electrolyte imbalance may increase the risk of QT prolongation. Therefore, caution is advisable during concurrent use of haloperidol and loop diuretics. In general, haloperidol should also be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Tramadol: (Major) Haloperidol can competitively inhibit the metabolism of tramadol by CYP2D6. Concurrent use of haloperidol and tramadol increases plasma levels of tramadol and decreases the concentration of the active tramadol metabolite. This may lead to decreased analgesic effects of tramadol and possibly increased tramadol-induced side effects, including seizures, due to increased tramadol concentrations and the decrease in seizure threshold caused by haloperidol. Additive CNS depression may also be seen with the concomitant use of tramadol and haloperidol.
Trandolapril; Verapamil: (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. Verapamil is a substrate and inhibitor of CYP3A4. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and substrates or inhibitors of CYP3A4 or CYP2D6. Elevated haloperidol concentrations occurring through inhibition of CYP2D6 or CYP3A4 may increase the risk of adverse effects, including QT prolongation.
Trazodone: (Major) Trazodone can prolong the QT/QTc interval at therapeutic doses. In addition, there are post-marketing reports of torsade de pointes (TdP). Therefore, the manufacturer recommends avoiding trazodone in patients receiving other drugs that increase the QT interval. Haloperidol has a possible risk for QT prolongation and TdP. Myoclonus, which responded to a serotonin antagonist, was reported in a patient taking trazodone with buspirone and haloperidol.
Treprostinil: (Moderate) In general, haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Triamterene: (Moderate) In general, haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Triazolam: (Moderate) Haloperidol can potentiate the actions of other CNS depressants, such as benzodiazepines, Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects.
Tricyclic antidepressants: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as tricyclic antidepressants (TCAs). Caution should be exercised with simultaneous use of these agents due to potential excessive CNS effects. Limited data suggest that haloperidol may inhibit the metabolism of some tricyclic antidepressants, however, the clinical significance of this interaction is uncertain. Haloperidol is an

inhibitor of hepatic CYP2D6, and coadministration with many TCAs (which are CYP2D6 substrates) may lead to elevated TCA serum concentrations, potentiating toxicity. Haloperidol has also been associated with a possible risk for QT prolongation and/or torsades de pointes, particularly when excessive doses are used or in overdose. Haloperidol should be used cautiously with other agents that may have this effect (e.g., tricyclic antidepressants).
Trifluoperazine: (Moderate) Trifluoperazine, a phenothiazine, is associated with a possible risk for QT prolongation. Trifluoperazine may increase the risk of QT prolongation if coadministered with drugs with a possible risk for QT prolongation, such as haloperidol. Co-administration of trifluoperazine with haloperidol may increase the risk of adverse effects such as drowsiness, dizziness, orthostatic hypotension, anticholinergic effects, extrapyramidal symptoms, neuroleptic malignant syndrome, or seizures. The likelihood of these pharmacodynamic interactions varies based upon the individual properties of the co-administered antipsychotic agent. Although the incidence of tardive dyskinesia from combination antipsychotic therapy has not been established and data are very limited, the risk appears to be increased during use of a conventional and atypical antipsychotic versus use of a conventional antipsychotic alone.
Trihexyphenidyl: (Moderate) The concurrent use of haloperidol with trihexyphenidyl is beneficial for many patients, as these anticholinergic agents treat drug-induced extrapyramidal symptoms. However, the anticholinergic effects of trihexyphenidyl may be additive to those of haloperidol, and may increase the incidence of dry mouth, constipation, or heat intolerance. Advise patients to promptly report gastrointestinal complaints, fever, or heat intolerance.
Triprolidine: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur.
Triptorelin: (Major) Androgen deprivation therapy (e.g., triptorelin) prolongs the QT interval; the risk may be increased with the concurrent use of drugs that may prolong the QT interval. Antipsychotic drugs with a possible risk for QT prolongation and TdP that should be used cautiously and with close monitoring with triptorelin include haloperidol. Additionally, some antipsychotics may induce hyperprolactinemia, resulting in down-regulatation of the number of pituitary GnRH receptors and may interfere with the response to triptorelin therapy.
Valproic Acid, Divalproex Sodium: (Major) Concomitant use of other CNS depressants, such as haloperidol, with valproic acid can cause additive CNS depression. Haloperidol, used concomitantly with valproic acid, can increase CNS depression and also can lower the seizure threshold, requiring change in the valproic acid dose.
Valsartan: (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Vandetanib: (Major) The manufacturer of vandetanib recommends avoiding coadministration with other drugs that prolong the QT interval due to an increased risk of QT prolongation and torsade de pointes (TdP). Vandetanib can prolong the QT interval in a concentration-dependent manner. TdP and sudden death have been reported in patients receiving vandetanib. QT prolongation and TdP have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. If coadministration is necessary, an ECG is needed, as well as more frequent monitoring of the QT interval. If QTcF is greater than 500 msec, interrupt vandetanib dosing until the QTcF is less than 450 msec; then, vandetanib may be resumed at a reduced dose.
Vardenafil: (Major) Therapeutic (10 mg) and supratherapeutic (80 mg) doses of vardenafil produces an increase in QTc interval (e.g., 4 to 6 msec calculated by individual QT correction). When vardenafil (10 mg) was given with gatifloxacin (400 mg), an additive effect on the QT interval was observed. The effect of vardenafil on the QT interval should be considered when prescribing the drug. Drugs with a possible risk for QT prolongation and TdP that should be used cautiously with vardenafil include haloperidol. QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. In addition, haloperidol is a substrate for CYP2D6. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and inhibitors of CYP2D6. Vardenafil is a CYP2D6 inhibitor. Monitor closely.
Vasodilators: (Moderate) In general, haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.
Vemurafenib: (Major) Vemurafenib has been associated with QT prolongation. If vemurafenib and another drug, such as haloperidol, that is associated with a possible risk for QT prolongation and torsade de pointes (TdP) must be coadministered, ECG monitoring is recommended; closely monitor the patient for QT interval prolongation. Also, haloperidol is a CYP2D6 and 3A4 substrate, while vemurafenib is a weak CYP2D6 inhibitor and a CYP3A4 substrate/inducer; therefore, altered concentrations of haloperidol may occur with concomitant use. Elevated haloperidol concentrations occurring through inhibition of CYP2D6 or CYP3A4 may increase the risk of adverse effects, including QT prolongation.
Venlafaxine: (Major) Caution is advisable during concurrent use of venlafaxine and haloperidol since both agents are associated with a possible risk of QT prolongation. In addition, venlafaxine is an inhibitor of CYP2D6, and concurrent use with CYP2D6 substrates, such as haloperidol, may result in increased plasma concentrations of such antipsychotics. In one case report, venlafaxine administered at 150 mg/day in 24 subjects decreased total oral clearance of a 2 mg dose of haloperidol by 42%, which resulted in a 70% increase in haloperidol AUC. In addition, the haloperidol Cmax increased 88% when coadministered with venlafaxine, but the haloperidol elimination half-life was unchanged.
Verapamil: (Moderate) In general, antipsychotics like haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension. Verapamil is a substrate and inhibitor of CYP3A4. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and substrates or inhibitors of CYP3A4 or CYP2D6. Elevated haloperidol concentrations occurring through inhibition of CYP2D6 or CYP3A4 may increase the risk of adverse effects, including QT prolongation.
Voriconazole: (Major) Caution is advised when administering voriconazole with drugs that are known to prolong the QT interval and are metabolized by CYP3A4, such as haloperidol. Haloperidol is primarily metabolized by CYP2D6. However, in patients that are lacking in CYP2D6 enzyme activity (slow metabolizers), the CYP3A4 enzyme may play a larger role in haloperidol metabolism. Concurrent use of voriconazole (a CYP3A4 inhibitor) with haloperidol may result in increased serum haloperidol concentrations. QT prolongation and torsade de pointes (TdP) have been observed during both voriconazole and haloperidol treatment. Voriconazole has also been associated with rare cases of cardiac arrest and sudden death; coadministration with haloperidol may increase this risk. If these drugs are given together, closely monitor for prolongation of the QT interval. Rigorous attempts to correct any electrolyte abnormalities (i.e., potassium, magnesium, calcium) should be made before initiating concurrent therapy.
Vorinostat: (Major) QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. According to the manufacturer of haloperidol, caution is advisable when prescribing the drug concurrently with medications known to prolong the QT interval, including vorinostat.
Warfarin: (Moderate) Haloperidol can decrease the anticoagulation effects of warfarin. If these drugs are coadministered, monitor INR and adjust warfarin doses as needed.
Zafirlukast: (Moderate) Zafirlukast is an inhibitor of CYP3A4, one of the isoenzymes responsible for the metabolism of haloperidol. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and substrates or inhibitors of CYP3A4. Until more data are available, it is advisable to closely monitor for adverse events when these medications are co-administered.
Zaleplon: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as anxiolytics, sedatives, and hypnotics, and they should be used cautiously in combination.
Ziconotide: (Moderate) Due to potentially additive effects, dosage adjustments may be necessary if ziconotide is used with a drug that has CNS depressant effects such as haloperidol. Coadministration of CNS depressants may increase drowsiness, dizziness, and confusion that are associated with ziconotide.
Ziprasidone: (Severe) Ziprasidone has been associated with a possible risk for QT prolongation and/or torsades de pointes. According to the manufacturer of ziprasidone, the drug is contraindicated with any drug that lists QT prolongation as a pharmacodynamic effect when this effect has been described within the contraindications or bolded or boxed warnings of the official labeling for such drugs. Haloperidol is associated with a possible risk for QT prolongation and TdP based on varying levels of documentation and is contraindicated with ziprasidone. In addition, coadministration of ziprasidone with haloperidol may increase the risk of adverse effects such as drowsiness, dizziness, orthostatic hypotension, anticholinergic effects, extrapyramidal symptoms, neuroleptic malignant syndrome, or seizures. The likelihood of these pharmacodynamic interactions varies based upon the individual properties of the co-administered antipsychotic agent. Although the incidence of tardive dyskinesia from combination antipsychotic therapy has not been established and data are very limited, the risk appears to be increased during use of a

conventional and atypical antipsychotic versus use of a conventional antipsychotic alone.
Zolpidem: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as anxiolytics, sedatives, and hypnotics, and they should be used cautiously in combination.
Zonisamide: (Moderate) Zonisamide may cause decreased sweating (oligohidrosis), elevated body temperature (hyperthermia), heat intolerance, or heat stroke. The manufacturer recommends caution in using concurrent drug therapies that may predispose patients to heat-related disorders such as antipsychotics. Monitor patients for heat intolerance, decreased sweating, or increased body temperature if zonisamide is used with any of these agents.

PREGNANCY AND LACTATION

Pregnancy

According to the manufacturers of the oral and injectable formulations, breast-feeding should be avoided during treatment with haloperidol. Haloperidol is excreted into breast milk. In one small study, developmental delays were reported in some nursing infants following combined use of haloperidol and chlorpromazine, while monotherapy did not result in this outcome. Conversely, in 2 women who received 5 mg/day of haloperidol plus olanzapine or amisulpride during pregnancy and breast-feeding, the breastfed infants exhibited normal development, and no adverse effects were noted during the 11 to 13 month follow-up period. In other case reports of breast-feeding during haloperidol monotherapy or combination therapy with imipramine or trihexyphenidyl and a haloperidol dose in the general range of 7.5 mg/day to 15 mg/day, age-appropriate development of the breastfed infants occurred during the follow-up period (range: 12 months to 8 years). Haloperidol may cause elevated prolactin levels and galactorrhea, and thus has the potential to alter proper lactation in some patients. Some data suggest that postnatal women are more sensitive to the prolactin-elevating effects of antipsychotics than nonpuerperal women. Due to individual variability in response to antipsychotics, it may be prudent to continue the existing regimen if ongoing treatment is deemed necessary during breast-feeding; however, alternate medications for consideration include atypical agents such as olanzapine or quetiapine. Data regarding the safety of atypical antipsychotics during breast-feeding are limited and chronic administration of any antipsychotic during breast-feeding should be avoided if possible. Regardless of the antipsychotic used, the nursing infant should be closely monitored for excessive drowsiness, lethargy, and developmental delays. Combination treatment with antipsychotics may increase the risk of these adverse events. Consider the benefits of breast-feeding, the risk of potential infant drug exposure, and the risk of an untreated or inadequately treated condition. If a breast-feeding infant experiences an adverse effect related to a maternally ingested drug, healthcare providers are encouraged to report adverse effects to the FDA.

MECHANISM OF ACTION

The precise mechanism of action of conventional antipsychotics, such as haloperidol, is unknown; however, the therapeutic effect in treating the positive symptoms of schizophrenia (e.g., hallucinations, delusions) is thought to occur from blockade of central postsynaptic dopamine (D-2) receptors in the mesolimbic pathway. By antagonizing dopamine in all areas of the brain, conventional antipsychotics are effective for treating the positive symptoms of schizophrenia, but can cause a variety of adverse effects. In addition, therapeutic effects on the negative symptoms (e.g., social withdrawal, blunted affect) and cognitive symptoms of schizophrenia relate to increased dopamine activity in the prefrontal cortex which may, in part, account for the general lack of improvement in these symptoms observed with D-2 blockers such as conventional agents. Antipsychotics appear to have neuroplastic effects, including synaptic plasticity (remodeling of synapses and development of new neuron connections) and neurogenesis (new neuron development), which may partially explain the delay in some of the therapeutic effects of antipsychotics. Induction of synaptic plasticity has been well-documented with haloperidol in the striatum, where the highest concentration of D-2 receptors exist.

In the nigrostriatal pathway, antipsychotic-induced dopamine blockade can lead to pseudoparkinsonism and other extrapyramidal symptoms (e.g., dystonic reactions, akathisia). Dopamine receptor blockade in the tuberoinfundibular tract results in prolactin release, which can lead to adverse effects related to hyperprolactinemia such as weight gain and menstrual irregularity. Haloperidol has a negligible affinity for muscarinic receptors, resulting in only weak anticholinergic effects. Haloperidol also has a weak affinity for alpha-1 and H-1 receptors, minimizing the likelihood of orthostatic hypotension, dizziness, reflex tachycardia, and sedation compared to many other antipsychotics.

PHARMACOKINETICS

Haloperidol is FDA approved for oral and intramuscular (immediate-release and decanoate) administration. Haloperidol injection is not approved for intravenous administration. If haloperidol is administered intravenously, the ECG should be monitored for QT prolongation and arrhythmias. Haloperidol decanoate dissolved in sesame oil is given by deep intramuscular injection, which results in slow and sustained release of haloperidol. Haloperidol is 92% plasma protein-bound, predominately to alpha-1-acid glycoprotein. It appears to exhibit extensive first pass metabolism. Haloperidol is extensively metabolized in the liver through N-dealkylation to inactive metabolites, and metabolism by glucuronidation also occurs. Reduction to hydroxyhaloperidol, an active metabolite, also occurs. CYP2D6 and CYP3A4 are the CYP isoenzymes involved in the metabolism. Slow metabolizers of CYP2D6 appear to be at increased risk of experiencing extrapyramidal symptoms due to delayed clearance of the drug. About 40% of a dose is excreted renally within 5 days, with 1% appearing as unchanged drug. Approximately 15% is eliminated through biliary excretion. The elimination half-life for immediate-release products ranges between 12—22 hours (average 16 hours) in adult patients.

A 2 mg oral dose would be approximately equivalent to 100 mg chlorpromazine, the prototype antipsychotic.

Affected cytochrome P450 (CYP450) isoenzymes and drug transporters: CYP2D6, CYP3A4
Haloperidol is partially metabolized by CYP2D6 and CYP3A4. Inhibition of one or more of these metabolic pathways may result in increased haloperidol concentrations and the potential for QT prolongation. Mild to moderate increases in haloperidol concentrations have been reported during concomitant use of haloperidol and substrates or inhibitors of CYP3A4 or CYP2D6. Significant reductions in haloperidol concentrations have occurred with use of some enzyme-inducing drugs. Some data suggest that haloperidol is a moderate inhibitor of CYP2D6.

Oral Route

Following oral administration in adults, systemic absorption occurs in 60—90 minutes. Peak plasma concentrations are attained in 4—6 hours. First-pass metabolism in the liver, and potentially other factors, reduces the bioavailability of haloperidol to approximately 40—60%. The elimination half-life ranges between 12—22 hours (average 16 hours) in adult patients.

Intravenous Route

Immediate-release lactate injection solution: This formulation is only approved for intramuscular administration; if administered intravenously, the ECG should be monitored for QT prolongation and arrhythmias.

Intramuscular Route

Immediate-release lactate injection solution: In adults, peak plasma concentrations occur in 20 to 40 minutes.

Decanoate depot in oil injection: Following deep intramuscular injection in adults, the plasma concentrations of haloperidol gradually rise; peak plasma concentrations are achieved after about 6 days, and decrease thereafter. Steady state is achieved after the third of fourth dose. The

apparent half-life of haloperidol decanoate is about 3 weeks. The relationship between dose of haloperidol decanoate and plasma haloperidol concentration is roughly linear for doses below 450 mg; however, it should be noted that the pharmacokinetics of haloperidol decanoate can be highly variable between patients.