CLASSES
ACTH and Analogs

DEA CLASS
Rx

DESCRIPTION
Parenteral adrenocorticotropic hormone (ACTH); highly purified and extracted from porcine pituitary glands
Repository injection primarily used in adults for multiple sclerosis; other corticosteroids usually preferred for other indications
In pediatric patients, repository injection primarily used for infantile spasms in infants and children less than 2 years

COMMON BRAND NAMES
H.P. Acthar

HOW SUPPLIED
H.P. Acthar Intramuscular Inj Sol: 1mL, 80U
H.P. Acthar Subcutaneous Inj Sol: 1mL, 80U

DOSAGE & INDICATIONS

For the treatment of infantile spasms.
Intramuscular dosage (repository corticotropin injection)
Infants and Children less than 2 years
75 units/m2/dose intramuscularly twice daily for 2 weeks is the FDA-approved regimen. The dose should then be tapered over a 2 week period to avoid adrenal insufficiency. The manufacturer suggests the following tapering schedule: 30 units/m2/dose intramuscularly every morning for 3 days, 15 units/m2/dose intramuscularly every morning for 3 days, and 10 units/m2/dose intramuscularly every morning for 6 days. Body surface area should be calculated with the following formula: BSA (m2) = the square root of ([height (cm) x weight (kg)]/3600). Various other non-FDA-approved regimens have been used off label. Low doses of 5 to 40 units/day intramuscularly for 1 to 6 weeks have been recommended by some neurologists, whereas others recommend larger doses of 40 to 160 units/day intramuscularly for 3 to 12 months. In 1 study, no major difference in efficacy was found between low doses for short periods and large doses for longer periods of time; however, hypertension was more common with the larger doses. In this study, the low-dose regimen was 20 units/day intramuscularly for 2 weeks. If the patient responded, the dose was tapered and discontinued over a 1-week period. If the patient did not respond, the dose was increased to 30 units/day intramuscularly for 4 weeks, then tapered and discontinued over a 1-week period. The high-dose regimen was 150 units/m2/day intramuscularly for 3 weeks; the dose was then tapered and discontinued over 9 weeks.

For the treatment of acute exacerbations of multiple sclerosis.
Intramuscular or Subcutaneous dosage (repository corticotropin injection)
Adults
80 to 120 units/day IM or subcutaneously for 2 to 3 weeks. It may be necessary to taper the dose.

For the adjunctive treatment of an acute episode or exacerbation of psoriatic arthritis, rheumatoid arthritis, juvenile rheumatoid arthritis (JRA)/juvenile idiopathic arthritis (JIA), and ankylosing spondylitis.
Intramuscular or Subcutaneous dosage (repository corticotropin injection)
Adults, Adolescents, and Children greater than 2 years
40 to 80 units intramuscularly or subcutaneously every 24 to 72 hours. Individualize the dose and dosing frequency after considering the disease severity, patient response, and plasma and urine corticosteroid concentrations. After prolonged use, a gradual taper may be necessary in order to avoid adrenal insufficiency or recurrent symptoms. Selected cases may require low-dose maintenance therapy.

For the treatment of symptomatic sarcoidosis.
Intramuscular or Subcutaneous dosage (repository corticotropin injection)
Adults, Adolescents, and Children greater than 2 years
40 to 80 units IM or subcutaneously every 24 to 72 hours. Individualize the dose and dosing frequency after considering the disease severity, patient response, and plasma and urine corticosteroid concentrations. After prolonged use, a gradual taper may be necessary in order to avoid adrenal insufficiency or recurrent symptoms.

For the treatment of ophthalmic diseases, such as keratitis, iritis, iridocyclitis, diffuse posterior uveitis, choroiditis, optic neuritis, chorioretinitis, and anterior segment inflammation.
Intramuscular or Subcutaneous dosage (repository corticotropin injection)

**Adults, Adolescents, and Children greater than 2 years**

40 to 80 units IM or subcutaneously every 24 to 72 hours. Individualize the dose and dosing frequency after considering the disease severity, patient response, and plasma and urine corticosteroid concentrations. After prolonged use, a gradual taper may be necessary in order to avoid adrenal insufficiency or recurrent symptoms.

**For the induction of diuresis or remission of proteinuria in the nephrotic syndrome.**

Intramuscular or subcutaneous dosage (repository corticotropin injection)

**Adults, Adolescents, and Children greater than 2 years**

40 to 80 units IM or subcutaneously every 24 to 72 hours. Individualize the dose and dosing frequency after considering the disease severity, patient response, and plasma and urine corticosteroid concentrations. After prolonged use, a gradual taper may be necessary in order to avoid adrenal insufficiency or recurrent symptoms.

**For the treatment of dermatologic and allergic states, including severe erythema multiforme, Stevens-Johnson syndrome, or serum sickness, or for collagen diseases such as systemic lupus erythematosus (SLE) or systemic dermatomyositis (polymyositis).**

Intramuscular or Subcutaneous dosage (repository corticotropin injection)

**Adults, Adolescents, and Children greater than 2 years**

40 to 80 units IM or subcutaneously every 24 to 72 hours. Individualize the dose and dosing frequency after considering the disease severity, patient response, and plasma and urine corticosteroid concentrations. After prolonged use, a gradual taper may be necessary in order to avoid adrenal insufficiency or recurrent symptoms.

**MAXIMUM DOSAGE**

**Adults**

80 units/day subcutaneous or IM for most conditions; up to 120 units/day IM for multiple sclerosis exacerbations.

**Geriatric**

80 units/day subcutaneous or IM for most conditions; up to 120 units/day IM for multiple sclerosis exacerbations.

**Adolescents**

80 units/day subcutaneous or IM.

**Children**

2 years and older: 80 units/day subcutaneously or IM. 
Less than 2 years: 150 units/m2/day IM.

**Infants**

150 units/m2/day IM.

**Neonates**

Safety and efficacy have not been established.

**DOSING CONSIDERATIONS**

**Hepatic Impairment**

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

**Renal Impairment**

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

**ADMINISTRATION**

**Injectable Administration**

Corticotropin, ACTH is administered parenterally.

Visually inspect parenteral products for particulate matter and discoloration prior to administration whenever solution and container permit.

**Intramuscular Administration**

Warm the repository gel to room temperature before administration. Do not over-pressurize the vial prior to withdrawing the drug. Inject deeply into a large muscle mass. Aspirate prior to injection to avoid injection into a blood vessel. Massage area following administration. Rotate sites of injection.

**Subcutaneous Administration**

Warm the repository gel to room temperature before administration. Do not over-pressurize the vial prior to withdrawing the drug. Inject subcutaneously, taking care not to inject intradermally.

**STORAGE**

H.P. Acthar:

- Refrigerate (between 36 and 46 degrees F)
CONTRAINDICATIONS / PRECAUTIONS

Corticosteroid hypersensitivity, porcine protein hypersensitivity

The use of corticotropin is contraindicated in patients with previous hypersensitivity to corticotropin therapy and those with porcine protein hypersensitivity. Although true corticosteroid hypersensitivity is rare, patients who have demonstrated a prior hypersensitivity reaction to corticotropin should not receive any form of corticotropin. It is possible, though also rare, that such patients will display cross-hypersensitivity to other corticosteroids. It is advisable that patients who have a hypersensitivity reaction to any corticosteroid undergo skin testing, which, although not a conclusive predictor, may help to determine if hypersensitivity to another corticosteroid exists. Such patients should be carefully monitored during and following the administration of any corticosteroid.

Intravenous administration

Corticotropin repository gel is contraindicated for intravenous administration.

Fungal infection, herpes infection, infection, ocular infection, tuberculosis

Due to suppression of the immune system, corticotropin should not be used in patients with infection caused by bacteria, viruses, or fungi that is not controlled by antimicrobials, unless it is a life-threatening situation. The use of corticotropin is contraindicated in patients with a systemic fungal infection, ocular herpes infection, or in very young pediatric patients with a suspected congenital infection. The use of corticotropin in patients with herpes simplex ocular infection can increase the risk of corneal perforation. Those patients with latent tuberculosis or a positive tuberculin skin test should be observed closely during therapy with corticotropin; if therapy is prolonged, initiate chemoprophylaxis.

Vaccination

Vaccination with live or live attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of corticotropin. Killed or inactivated vaccines should be given with caution during therapy with corticotropin because corticotropin inhibits antibody response after vaccination and neurologic reactions may be aggravated.

Cardiac disease, heart failure, hypertension

Corticotropin is contraindicated in patients with uncontrolled hypertension or congestive heart failure and should be used with caution in patients any degree of hypertension or heart failure. Corticotropin should be used cautiously in patients with other types of cardiac disease due to its propensity to cause water retention and hypotension and to lower serum potassium concentrations. Patients may require potassium supplementation while receiving corticotropin.

Diverticulitis, peptic ulcer disease, ulcerative colitis

Since corticotropin stimulates the production of endogenous corticosteroids, the drug should be used with caution in patients with GI disease, including diverticulitis, ulcerative colitis, or intestinal anastomosis due to a risk of perforation. The use of corticotropin is contraindicated in patients with peptic ulcer disease.

Scleroderma, surgery

The use of corticotropin is contraindicated in patients with scleroderma or in patients that have had recent surgery.

Adrenocortical insufficiency, Cushing's syndrome, hypercortisolism, hypothalamic-pituitary-adrenal (HPA) suppression

Corticotropin is contraindicated in patients with primary adrenal insufficiency, hypercortisolism, or any condition associated with these disorders. Prolonged therapy with corticotropin causes hypothalamic-pituitary-adrenal (HPA) suppression due to inhibition of corticotropin release from the pituitary. Patients on long-term therapy may require additional doses of corticosteroids when subjected to stress such as illness, infection, surgery, or trauma. Abrupt discontinuation of corticotropin, especially after prolonged therapy, can lead to adrenal insufficiency. Patients should be monitored for symptoms of adrenal insufficiency after corticotropin therapy is discontinued; these symptoms include fatigue, anorexia, weakness, hyperpigmentation, weight loss, hypotension, and abdominal pain. Parents and caregivers of pediatric patients receiving corticotropin for the treatment of infantile spasms should be informed of the possibility of adrenal insufficiency when the drug is discontinued and instructed to monitor for these symptoms. Adrenal insufficiency can be minimized by tapering of the corticotropin dose prior to discontinuation. Glucocorticoids can also cause or aggravate Cushing's syndrome and therefore should be avoided in patients with Cushing's disease.

Myasthenia gravis, psychosis, seizure disorder

Corticotropin should be used with extreme caution in patients with certain chronic or comorbid conditions because the drug may exacerbate these conditions. These include behavioral disorders such as psychosis or emotional instability and neurologic diseases such as myasthenia gravis or seizure disorder.

Diabetes mellitus, hypothyroidism

Corticotropin should be used with caution in patients with certain endocrine conditions such as diabetes mellitus and hypothyroidism. Corticotropin may exacerbate diabetes mellitus; diabetic patients may have an increased requirement for insulin or oral hypoglycemics. Monitor patients for hyperglycemia during and for a period of time after corticotropin therapy. Patients with hypothyroidism can have an exaggerated response to corticotropin or exogenous corticosteroids; any corticosteroid should be used with caution in these patients.

Hypernatremia, hypokalemia, renal impairment

Due to the sodium-retaining, fluid-retaining, and potassium-wasting properties of the drug, corticotropin should be used with caution in patients with renal impairment, hypokalemia, hypernatremia, or other patients who may be sensitive to fluid/electrolyte disturbances.

Thromboembolic disease

Use corticotropin cautiously in patients with thromboembolic disease because this drug rarely has been reported to increase blood coagulability and to precipitate intravascular thrombosis, thrombophlebitis, and thromboembolism.

Geriatric, osteoporosis, postmenopausal females

Prolonged therapy with corticotropin can cause atrophy of the bone protein matrix due to protein catabolism. This atrophy can cause osteoporosis, fractures, aseptic necrosis of femoral and humoral heads, and pathologic fractures of long bones. Corticotropin is contraindicated in patients with pre-existing osteoporosis. Use cautiously in geriatric, debilitated, and postmenopausal females.

Children, infants, neonates

The use of corticotropin is contraindicated in infants with a suspected congenital infection. Infants and children < 2 years experience a high rate of infections while receiving corticotropin therapy for infantile spasms; monitor patients carefully for signs and symptoms of infection. Additionally, due to potentially negative effects on growth and development, corticotropin should not be used for prolonged periods in infants, children, or adolescents. Corticotropin may cause retardation of bone growth. In addition, prolonged therapy with corticotropin can cause atrophy of the bone.

H.P. Acthar (corticotropin) dose, indications, adverse effects, interactions... from PDR.net

Pregnancy
Corticotropin, ACTH is classified as FDA pregnancy risk category C. Safe use of corticotropin during human pregnancy has not been established. Corticotropin has been shown to have an embryocidal effect and to cause fetal damage in animals. It also causes the release of cortisol and endogenous corticosteroids. Per the manufacturer, corticotropin use should be avoided during pregnancy unless the potential therapeutic benefit justifies the added risk to the fetus. Adrenocortical disease during pregnancy is relatively rare as most cases are diagnosed before a woman becomes pregnant, but ACTH stimulated normal cortisol values have been established for each trimester. Adrenal disease may cause significant maternal and fetal morbidity, so accurate and rapid diagnosis is important. The use of cosyntropin to confirm the diagnosis of adrenal insufficiency during pregnancy, when suspected, is described in the literature.

Breast-feeding
It is not known whether corticotropin, ACTH is excreted in human milk. Because many drugs are excreted in human milk and due to the potential for serious adverse reactions in nursing infants, the manufacturer states that a decision should be made whether to discontinue breast-feeding or to discontinue the drug, taking into account the importance of the drug to the mother and the indication for use. However, due to its large molecular weight and short half-life of only 10 to 15 minutes, corticotropin, ACTH is unlikely to appear in human milk. It is unlikely that corticotropin, ACTH would be absorbed by the infant because it would probably be degraded in the infant's gastrointestinal tract. Animal data suggests an increase in breast milk cortisol levels might be expected after administration of corticotropin to a nursing mother. However, if corticotropin is required in the mother, it is not a reason to discontinue breast-feeding. Alternative therapies to consider include other corticosteroids, such as prednisone and methylprednisolone. Prednisone concentrations in breast milk are low, and no adverse effects have been reported in the breast-fed infant with maternal use of any corticosteroid during breast-feeding; prednisone is generally considered compatible to use during lactation. 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 administered drug, healthcare providers are encouraged to report the adverse effect to the FDA.

Severe
seizures / Delayed / 3.0-12.0
vasculitis / Delayed / Incidence not known
skin atrophy / Delayed / Incidence not known
pancreatitis / Delayed / Incidence not known
anaphylactic shock / Rapid / Incidence not known
scarlatiniform exanthema / Rapid / Incidence not known
ocular hypertension / Delayed / Incidence not known
heart failure / Delayed / Incidence not known
bone fractures / Delayed / Incidence not known
avascular necrosis / Delayed / Incidence not known
papilledema / Delayed / Incidence not known
intracranial bleeding / Delayed / Incidence not known

Moderate
Cushing's syndrome / Delayed / 3.0-22.0
hypertension / Early / 11.0-19.0
constipation / Delayed / 5.0-5.0
candidiasis / Delayed / 2.0
erythema / Early / Incidence not known
esophagitis / Delayed / Incidence not known
wheezing / Rapid / Incidence not known
exophthalmos / Delayed / Incidence not known
cataracts / Delayed / Incidence not known
sodium retention / Delayed / Incidence not known
hypophosphatemia / Delayed / Incidence not known
hypernatremia / Delayed / Incidence not known
hypokalemia / Delayed / Incidence not known
hypocalcemia / Delayed / Incidence not known
metabolic alkalosis / Delayed / Incidence not known
depression / Delayed / Incidence not known
sodium retention / Delayed / Incidence not known
euphoria / Early / Incidence not known
psychosis / Early / Incidence not known
hyperglycemia / Delayed / Incidence not known
withdrawal / Early / Incidence not known
hypothalamic-pituitary-adrenal (HPA) suppression / Delayed / Incidence not known
myopathy / Delayed / Incidence not known
osteoporosis / Delayed / Incidence not known
impaired wound healing / Delayed / Incidence not known
subdural hematoma / Early / Incidence not known
EEG changes / Delayed / Incidence not known
pseudotumor cerebri / Delayed / Incidence not known

Mild
infection / Delayed / 20.0-46.0
irritability / Delayed / 7.0-19.0
acne vulgaris / Delayed / 14.0-14.0
diarrhea / Early / 3.0-14.0
rash / Early / 8.0-8.0
fever / Early / 5.0-8.0
vomiting / Early / 3.0-5.0
nasal congestion / Early / 1.0-5.0
appetite stimulation / Delayed / 0-5.0
weight gain / Delayed / 1.0-3.0
injection site reaction / Rapid / Incidence not known
skin hyperpigmentation / Delayed / Incidence not known
amenorrhea / Delayed / Incidence not known
hyperhidrosis / Delayed / Incidence not known
e cachexia / Delayed / Incidence not known
petechiae / Delayed / Incidence not known
hirsutism / Delayed / Incidence not known
dyspepsia / Early / Incidence not known
nausea / Early / Incidence not known
urticaria / Rapid / Incidence not known
pruritus / Rapid / Incidence not known
dizziness / Early / Incidence not known
insomnia / Early / Incidence not known
emotional lability / Early / Incidence not known
menstrual irregularity / Delayed / Incidence not known
myalgia / Early / Incidence not known
anorexia / Delayed / Incidence not known
weakness / Early / Incidence not known
headache / Early / Incidence not known
vertigo / Early / Incidence not known

**DRUG INTERACTIONS**

**Abatacept:** (Moderate) Concomitant use of immunosuppressives, as well as long-term corticosteroids, may potentially increase the risk of serious infection in abatacept-treated patients. Advise patients taking abatacept to seek immediate medical advice if they develop signs and symptoms suggestive of infection.

**Acetaminophen; Aspirin, ASA; Caffeine:** (Moderate) Salicylates or NSAIDs should be used cautiously in patients receiving corticosteroids. While there is controversy regarding the ulcercogenic potential of corticosteroids alone, concomitant administration of corticosteroids with aspirin may increase the GI toxicity of aspirin and other non-acetylated salicylates. Withdrawal of corticosteroids can result in increased plasma concentrations of salicylate and possible toxicity. Concomitant use of corticosteroids may increase the risk of adverse GI events due to NSAIDs. Although some patients may need to be given corticosteroids and NSAIDs concomitantly, which can be done successfully for short periods of time without sequelae, prolonged coadministration should be avoided.

**Acetaminophen; Caffeine; Magnesium Salicylate; Phenyltoloxamine:** (Moderate) Salicylates or NSAIDs should be used cautiously in patients receiving corticosteroids. While there is controversy regarding the ulcerogenic potential of corticosteroids alone, concomitant administration of corticosteroids with aspirin may increase the GI toxicity of aspirin and other non-acetylated salicylates. Withdrawal of corticosteroids can result in increased plasma concentrations of salicylate and possible toxicity. Concomitant use of corticosteroids may increase the risk of adverse GI events due to NSAIDs. Although some patients may need to be given corticosteroids and NSAIDs concomitantly, which can be done successfully for short periods of time without sequelae, prolonged coadministration should be avoided.

**Acetaminophen; Chlorpheniramine; Dextromethorphan; Phenylephrine:** (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.

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**Acetaminophen; Hydrochlorothiazide, HCTZ:** (Moderate) Additive hypokalemia may occur when non-potassium sparing diuretics, including thiazide diuretics, are coadministered with other drugs with a significant risk of hypokalemia, such as corticosteroids. Monitoring serum potassium levels and cardiac function is advised, and potassium supplementation may be required.

**Aliskiren; Hydrochlorothiazide, HCTZ:** (Moderate) Additive hypokalemia may occur when non-potassium sparing diuretics, including thiazide diuretics, are coadministered with other drugs with a significant risk of hypokalemia, such as corticosteroids. Monitoring serum potassium levels and cardiac function is advised, and potassium supplementation may be required.

**Alogliptin; Metformin:** (Moderate) Monitor patients receiving antidiabetic agents closely for worsening glycemic control when corticosteroids are
instituted and for signs of hypoglycemia when corticosteroids are discontinued. Systemic and inhaled corticosteroids are known to increase blood glucose and worsen glycemic control in patients taking antidiabetic agents. The main risk factors for impaired glucose tolerance due to corticosteroids are the dose of steroid and duration of treatment. Corticosteroids stimulate hepatic glucose production and inhibit peripheral glucose uptake into muscle and fatty tissues, producing insulin resistance. Decreased insulin production may occur in the pancreas due to a direct effect on pancreatic beta cells.

Alcohol: (Moderate) Concomitant use of alcohol with other agents which cause bone marrow or immune suppression such as corticosteroids may result in additive effects.

Amphenonium Chloride: (Minor) Concomitant use of amphenonium with other agents may result in synergistic effects.

Amiloride; Hydrochlorothiazide, HCTZ: (Moderate) Concomitant use of these drugs may result in additive effects.

Amphotericin B cholesteryl sulfate complex (ABCD): (Moderate) Concomitant use of amphotericin B with other drugs may result in additive effects.

Ambenonium Chloride: (Minor) Concomitant use of ambenonium with other agents may result in additive effects.

Amyl nitrite: (Moderate) Concomitant use of amyl nitrite with other agents may result in additive effects.

Ampicillin: (Moderate) Concomitant use of ampicillin with other agents may result in additive effects.

Ampicillin sodium: (Moderate) Concomitant use of ampicillin sodium with other agents may result in additive effects.

Amperocin B cholosteryl sulfate complex (ABCD): (Moderate) Concomitant use of amperocin B with other agents may result in additive effects.

Ampromide: (Moderate) Concomitant use of ampromide with other agents may result in additive effects.

Ampromide sulfate: (Moderate) Concomitant use of ampromide sulfate with other agents may result in additive effects.

Ampromide tartrate: (Moderate) Concomitant use of ampromide tartrate with other agents may result in additive effects.

Ampromide tosylate: (Moderate) Concomitant use of ampromide tosylate with other agents may result in additive effects.

Amrinone: (Moderate) Concomitant use of amrinone with other agents may result in additive effects.

Aminocapric acid: (Moderate) Concomitant use of aminocapric acid with other agents may result in additive effects.

Aminocaproic acid: (Moderate) Concomitant use of aminocaproic acid with other agents may result in additive effects.

Aminocaproic acid sodium: (Moderate) Concomitant use of aminocaproic acid sodium with other agents may result in additive effects.

Aminoguanidine: (Moderate) Concomitant use of aminoguanidine with other agents may result in additive effects.

Aminoguanidine hydrochloride: (Moderate) Concomitant use of aminoguanidine hydrochloride with other agents may result in additive effects.

Aminoguanidine sulfate: (Moderate) Concomitant use of aminoguanidine sulfate with other agents may result in additive effects.

Aminoguanidine tosylate: (Moderate) Concomitant use of aminoguanidine tosylate with other agents may result in additive effects.

Aminoguanidine threonine: (Moderate) Concomitant use of aminoguanidine threonine with other agents may result in additive effects.

Aminoguanidine threonine hydrochloride: (Moderate) Concomitant use of aminoguanidine threonine hydrochloride with other agents may result in additive effects.

Aminoguanidine threonine sulfate: (Moderate) Concomitant use of aminoguanidine threonine sulfate with other agents may result in additive effects.

Aminoguanidine threonine thiosulfate: (Moderate) Concomitant use of aminoguanidine threonine thiosulfate with other agents may result in additive effects.

Aminoguanidine threonine trihydrochloride: (Moderate) Concomitant use of aminoguanidine threonine trihydrochloride with other agents may result in additive effects.

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Aminoguanidine trihydrochloride sulfate: (Moderate) Concomitant use of aminoguanidine trihydrochloride sulfate with other agents may result in additive effects.

Aminoguanidine trihydrochloride thiosulfate: (Moderate) Concomitant use of aminoguanidine trihydrochloride thiosulfate with other agents may result in additive effects.

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Aminoguanidine threonine trihydrochloride: (Moderate) Concomitant use of aminoguanidine threonine trihydrochloride with other agents may result in additive effects.

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Aminoguanidine trihydrochloride su...
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Aspirin, ASA; Metoprolol: (Moderate) Additive hypokalemia may occur when non-potassium sparing diuretics, including thiazide diuretics, are coadministered with other drugs with a significant risk of hypokalemia, such as corticosteroids. Monitoring serum potassium levels and cardiac function is advised, and potassium supplementation may be required.

Atropine; Benzoic Acid; Hyoscyamine; Methenamine; Methylene Blue; Phenyl Salicylate: (Moderate) Additive hypokalemia may occur when non-potassium sparing diuretics, including thiazide diuretics, are coadministered with other drugs with a significant risk of hypokalemia, such as corticosteroids. Monitoring serum potassium levels and cardiac function is advised, and potassium supplementation may be required.
GI toxicity of aspirin and other non-acetylated salicylates. Withdrawal of corticosteroids can result in increased plasma concentrations of salicylate and possible toxicity. Concomitant use of corticosteroids may increase the risk of adverse GI events due to NSAIDs. Although some patients may need to be given corticosteroids and NSAIDs concomitantly, which can be done successfully for short periods of time without sequelae, prolonged coadministration should be avoided.

**Bismuth Subsalicylate; Metronidazole; Tetracycline:** (Moderate) Salicylates or NSAIDs should be used cautiously in patients receiving corticosteroids. There is cardiovascular and gastrointestinal stimulation following the administration of corticosteroids with aspirin may increase the GI toxicity of aspirin and other non-acetylated salicylates. Withdrawal of corticosteroids can result in increased plasma concentrations of aspirin and possible toxicity. Concomitant use of corticosteroids may increase the risk of adverse GI events due to NSAIDs. Although some patients may need to be given corticosteroids and NSAIDs concomitantly, which can be done successfully for short periods of time without sequelae, prolonged coadministration should be avoided.

**Chlorambucil:** (Moderate) Additive hypokalemia may occur when non-potassium sparing diuretics, including thiazide diuretics, are coadministered with other drugs with a significant risk of hypokalemia, such as corticosteroids. Monitoring serum potassium levels and cardiac function is advised, and potassium supplementation may be required.

**Bivalirudin:** (Moderate) Concomitant use of systemic sodium chloride, especially at high doses, and corticosteroids may result in sodium and fluid retention. Corticosteroids may increase serum sodium levels from sodium-containing medications and other sodium supplements. Carefully monitor sodium concentrations and fluid status if sodium-containing drugs and corticosteroids must be used together.

**Bortezomib:** (Minor) Because systemically administered corticosteroids exhibit immunosuppressive effects when given in high doses and/or for extended periods, additive effects may be seen with other immunosuppressive or antineoplastic agents.

**Brompheniramine; Carbamazepine; Phenylephrine:** (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.

**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 systemic corticosteroids. The manufacturer recommends low initial dosing and slow dosage titration if these combinations must be used; the patient should be closely monitored.

**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 systemic corticosteroids. The manufacturer recommends low initial dosing and slow dosage titration if these combinations must be used; the patient should be closely monitored.

**Calcium Carbonate:** (Moderate) Calcium absorption is reduced when calcium carbonate is taken concomitantly with systemic corticosteroids. Systemic corticosteroids induce a negative calcium balance by inhibiting intestinal calcium absorption as well as by increasing renal calcium losses. The mechanism by which these drugs inhibit calcium absorption in the intestine is likely to involve a direct inhibition of absorptive cell function.

**Calcium Carbonate; Magnesium Hydroxide:** (Moderate) Calcium absorption is reduced when calcium carbonate is taken concomitantly with systemic corticosteroids. Systemic corticosteroids induce a negative calcium balance by inhibiting intestinal calcium absorption as well as by increasing renal calcium losses. The mechanism by which these drugs inhibit calcium absorption in the intestine is likely to involve a direct inhibition of absorptive cell function.

**Calcium Carbonate; Risedronate:** (Moderate) Calcium absorption is reduced when calcium carbonate is taken concomitantly with systemic corticosteroids. Systemic corticosteroids induce a negative calcium balance by inhibiting intestinal calcium absorption as well as by increasing renal calcium losses. The mechanism by which these drugs inhibit calcium absorption in the intestine is likely to involve a direct inhibition of absorptive cell function.

**Calcium; Vitamin D:** (Moderate) Calcium absorption is reduced when calcium carbonate is taken concomitantly with systemic corticosteroids. Systemic corticosteroids induce a negative calcium balance by inhibiting intestinal calcium absorption as well as by increasing renal calcium losses. The mechanism by which these drugs inhibit calcium absorption in the intestine is likely to involve a direct inhibition of absorptive cell function.
corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.

Chlorpheniramine; Phenylephrine: (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.

Chlorpropamide: (Moderate) Monitor patients receiving antidiabetic agents closely for worsening glycemic control when corticosteroids are instituted and for signs of hypoglycemia when corticosteroids are discontinued. Systemic and inhaled corticosteroids are known to increase blood glucose and worsen glycemic control in patients taking antidiabetic agents. The main risk factors for impaired glucose tolerance due to corticosteroids are the dose of steroid and duration of treatment. Corticosteroids stimulate hepatic glucose production and inhibit peripheral glucose uptake into muscle and fatty tissues, producing insulin resistance. Decreased insulin production may occur in the pancreas due to a direct effect on pancreatic beta cells.

Chlorpheniramine; Phenylephrine: (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.

Chlorpropramide: (Moderate) Monitor patients receiving antidiabetic agents closely for worsening glycemic control when corticosteroids are instituted and for signs of hypoglycemia when corticosteroids are discontinued. Systemic and inhaled corticosteroids are known to increase blood glucose and worsen glycemic control in patients taking antidiabetic agents. The main risk factors for impaired glucose tolerance due to corticosteroids are the dose of steroid and duration of treatment. Corticosteroids stimulate hepatic glucose production and inhibit peripheral glucose uptake into muscle and fatty tissues, producing insulin resistance. Decreased insulin production may occur in the pancreas due to a direct effect on pancreatic beta cells.

Chlorpheniramine; Phenylephrine: (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.

Chlorpheniramine; Phenylephrine: (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.

Chlorpheniramine; Phenylephrine: (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.

Chlorpheniramine; Phenylephrine: (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.

Chlorpheniramine; Phenylephrine: (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.

Chlorpheniramine; Phenylephrine: (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.

Chlorpheniramine; Phenylephrine: (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.

Chlorpheniramine; Phenylephrine: (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.

Chlorpheniramine; Phenylephrine: (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.

Chlorpheniramine; Phenylephrine: (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.

Chlorpheniramine; Phenylephrine: (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.
Diphenhydramine; Phenylephrine: (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.

Dofetilide: (Major) Corticosteroids can increase in blood pressure, sodium and water retention, and hypokalemia, predisposing patients to interactions with certain other medications. Corticosteroid-induced hypokalemia could also enhance the proarrhythmic effects of dofetilide.

Doxaxurium: (Moderate) Caution and close monitoring are advised if corticosteroids and neuromuscular blockers are used together, particularly for those receiving enhanced neuromuscular blocking effects. In such patients, a peripheral nerve stimulator may be of value in monitoring the response. Concurrent use may increase the risk of acute myopathy. This acute myopathy is generalized, may involve ocular and respiratory muscles, and may result in quadriaparesis. Elevation of creatine kinase may occur. Clinical improvement or recovery after stopping corticosteroids may require weeks to years.

Droperidol: (Moderate) Caution is advised when using droperidol in combination with corticosteroids which may lead to electrolyte abnormalities, especially hypokalemia or hypomagnesemia, as such abnormalities may increase the risk for QT prolongation or cardiac arrhythmias.

Dulaglutide: (Moderate) Monitor patients receiving antidiabetic agents closely for worsening glycemic control when corticosteroids are instituted and for signs of hypoglycemia when corticosteroids are discontinued. Systemic and inhaled corticosteroids are known to increase blood glucose and worsen glycemic control in patients taking antidiabetic agents. The main risk factors for impaired glucose tolerance due to corticosteroids are the dose of steroid and duration of treatment. Corticosteroids stimulate hepatic glucose production and inhibit peripheral glucose uptake into muscle and fatty tissues, producing insulin resistance. Decreased insulin production may occur in the pancreas due to a direct effect on pancreatic beta cells.

Echinacea: (Moderate) Echinacea possesses immunostimulatory activity and may theoretically reduce the response to immunosuppressant drugs like corticosteroids. For some patients who are using corticosteroids for serious illness, such as cancer or organ transplant, this potential interaction may result in increased avoidable occurrence of Echinacea. Although documentation is lacking, coadministration of echinacea with immunosuppressants is not recommended by some dependent resources.

Econazole: (Minor) In vitro studies indicate that corticosteroids inhibit the antifungal activity of econazole against C. albicans in a concentration-dependent manner. When the concentration of the corticosteroid was equal to or greater than that of econazole on a weight basis, the antifungal activity of econazole was substantially inhibited. When the corticosteroid concentration was one-tenth that of econazole, no inhibition of antifungal activity was observed.

Efaluzumab: (Major) Patients receiving immunosuppressives should not receive concurrent therapy with efaluzumab because of the possibility of increased infections and malignancies.

Empagliflozin: (Moderate) Monitor patients receiving antidiabetic agents closely for worsening glycemic control when corticosteroids are instituted and for signs of hypoglycemia when corticosteroids are discontinued. Systemic and inhaled corticosteroids are known to increase blood glucose and worsen glycemic control in patients taking antidiabetic agents. The main risk factors for impaired glucose tolerance due to corticosteroids are the dose of steroid and duration of treatment. Corticosteroids stimulate hepatic glucose production and inhibit peripheral glucose uptake into muscle and fatty tissues, producing insulin resistance. Decreased insulin production may occur in the pancreas due to a direct effect on pancreatic beta cells.

Empagliflozin; Linagliptin: (Moderate) Monitor patients receiving antidiabetic agents closely for worsening glycemic control when corticosteroids are instituted and for signs of hypoglycemia when corticosteroids are discontinued. Systemic and inhaled corticosteroids are known to increase blood glucose and worsen glycemic control in patients taking antidiabetic agents. The main risk factors for impaired glucose tolerance due to corticosteroids are the dose of steroid and duration of treatment. Corticosteroids stimulate hepatic glucose production and inhibit peripheral glucose uptake into muscle and fatty tissues, producing insulin resistance. Decreased insulin production may occur in the pancreas due to a direct effect on pancreatic beta cells.

Empagliflozin; Metformin: (Moderate) Monitor patients receiving antidiabetic agents closely for worsening glycemic control when corticosteroids are instituted and for signs of hypoglycemia when corticosteroids are discontinued. Systemic and inhaled corticosteroids are known to increase blood glucose and worsen glycemic control in patients taking antidiabetic agents. The main risk factors for impaired glucose tolerance due to corticosteroids are the dose of steroid and duration of treatment. Corticosteroids stimulate hepatic glucose production and inhibit peripheral glucose uptake into muscle and fatty tissues, producing insulin resistance. Decreased insulin production may occur in the pancreas due to a direct effect on pancreatic beta cells.

Ephedrine: (Moderate) Ephedrine may enhance the metabolic clearance of corticosteroids. Decreased blood concentrations and lessened physiologic activity may necessitate an increase in corticosteroid dosage.

Eprosartan; Hydrochlorothiazide, HCTZ: (Moderate) Additive hypotension may occur when non-potassium sparing diuretics, including thiazide diuretics, are administered with other drugs with a significant risk of hypotension, such as corticosteroids. Monitoring serum potassium levels and cardiac function is advised, and potassium supplementation may be required.

Enalapril; Hydrochlorothiazide, HCTZ: (Moderate) Additive hypotension may occur when non-potassium sparing diuretics, including thiazide diuretics, are administered with other drugs with a significant risk of hypotension, such as corticosteroids. Monitoring serum potassium levels and cardiac function is advised, and potassium supplementation may be required.

Eprosartan: (Moderate) Additive hypotension may occur when non-potassium sparing diuretics, including thiazide diuretics, are administered with other drugs with a significant risk of hypotension, such as corticosteroids. Monitoring serum potassium levels and cardiac function is advised, and potassium supplementation may be required.

Eptingliflozin: (Moderate) Monitor patients receiving antidiabetic agents closely for worsening glycemic control when corticosteroids are instituted and for signs of hypoglycemia when corticosteroids are discontinued. Systemic and inhaled corticosteroids are known to increase blood glucose and worsen glycemic control in patients taking antidiabetic agents. The main risk factors for impaired glucose tolerance due to corticosteroids are the dose of steroid and duration of treatment. Corticosteroids stimulate hepatic glucose production and inhibit peripheral glucose uptake into muscle and fatty tissues, producing insulin resistance. Decreased insulin production may occur in the pancreas due to a direct effect on pancreatic beta cells.

Eprosartan: (Moderate) Additive hypotension may occur when non-potassium sparing diuretics, including thiazide diuretics, are administered with other drugs with a significant risk of hypotension, such as corticosteroids. Monitoring serum potassium levels and cardiac function is advised, and potassium supplementation may be required.

Ertugliflozin; Metformin: (Moderate) Monitor patients receiving antidiabetic agents closely for worsening glycemic control when corticosteroids are instituted and for signs of hypoglycemia when corticosteroids are discontinued. Systemic and inhaled corticosteroids are known to increase blood glucose and worsen glycemic control in patients taking antidiabetic agents. The main risk factors for impaired glucose tolerance due to corticosteroids are the dose of steroid and duration of treatment. Corticosteroids stimulate hepatic glucose production and inhibit peripheral glucose uptake into muscle and fatty tissues, producing insulin resistance. Decreased insulin production may occur in the pancreas due to a direct effect on pancreatic beta cells.

Ertugliflozin; Sitagliptin: (Moderate) Monitor patients receiving antidiabetic agents closely for worsening glycemic control when corticosteroids are instituted and for signs of hypoglycemia when corticosteroids are discontinued. Systemic and inhaled corticosteroids are known to increase blood glucose and worsen glycemic control in patients taking antidiabetic agents. The main risk factors for impaired glucose tolerance due to corticosteroids are the dose of steroid and duration of treatment. Corticosteroids stimulate hepatic glucose production and inhibit peripheral glucose uptake into muscle and fatty tissues, producing insulin resistance. Decreased insulin production may occur in the pancreas due to a direct effect on pancreatic beta cells.

Estramustine: (Minor) Because systemically administered corticosteroids exhibit immunosuppressive effects when given in high doses and/or for extended periods, additive effects may be seen with other immunosuppressives or antineoplastic agents.

Estrogens: Estrogens have been shown to improve the control of corticosteroid binding globulin (CBG), leading to increased total circulating corticosteroids, although the free concentrations of these hormones may be lower; the clinical significance is not known. Estrogens are CYP3A4 substrates and demethasone is a CYP3A4 inducer; concomitant use may decrease the clinical efficacy of estrogens. Patients should be monitored for signs of decreased clinical effects of estrogens (e.g., breakthrough bleeding), oral contraceptives, or non-oral contraceptives if these drugs are used together.

Exenatide: (Moderate) Monitor patients receiving antidiabetic agents closely for worsening glycemic control when corticosteroids are instituted and for signs of hypoglycemia when corticosteroids are discontinued. Systemic and inhaled corticosteroids are known to increase blood glucose and worsen glycemic control in patients taking antidiabetic agents. The main risk factors for impaired glucose tolerance due to corticosteroids are the dose of steroid and duration of treatment. Corticosteroids stimulate hepatic glucose production and inhibit peripheral glucose uptake into muscle and fatty tissues, producing insulin resistance. Decreased insulin production may occur in the pancreas due to a direct effect on pancreatic beta cells.

Flunazone: (Moderate) Concomitant use of systemic sodium chloride, especially at high doses, and corticosteroids may result in sodium and fluid retention. Assess sodium chloride intake from all sources, including intake from sodium-containing intravenous fluids and antibiotic admixtures. Carefully monitor sodium concentrations and fluid status if sodium-containing drugs and corticosteroids must be used together.

Fluoromethyzone: (Moderate) Coadministration of corticosteroids and fluoromethyzone may increase the risk of edema, especially in patients with
underlying cardiac or hepatic disease. Corticosteroids with greater mineralocorticoid activity, such as fludrocortisone, may be more likely to cause edema. Administer these drugs in combination with caution.

Fosinopril; Hydrochlorothiazide, HCTZ: (Moderate) Additive hypokalemia may occur when non-potassium sparing diuretics, including thiazide diuretics, are coadministered with other drugs with a significant risk of hypokalemia, such as corticosteroids. Monitoring serum potassium levels and cardiac function is advised, and potassium supplementation may be required.

Gallamine: (Moderate) Corticosteroids may accentuate the electrolyte loss associated with diuretic therapy resulting in hypokalemia. Also, corticosteroid may cause calcium loss and sodium and fluid retention. Manitol itself can cause hypokalemia. Close monitoring of electrolytes should occur in patients receiving these drugs concomitantly.

Gentamicin: (Moderate) Concomitant use of systemic sodium chloride, especially at high doses, and corticosteroids may result in sodium and fluid retention. Assess sodium chloride intake from all sources, including intake from sodium-containing intravenous fluids and antibiotic admixtures. Carefully monitor sodium concentrations and fluid status if sodium-containing drugs and corticosteroids must be used together.

Glibenclamide; Hydrochlorothiazide, HCTZ: (Moderate) Additive hypokalemia may occur when non-potassium sparing diuretics, including thiazide diuretics, are coadministered with other drugs with a significant risk of hypokalemia, such as corticosteroids. Monitoring serum potassium levels and cardiac function is advised, and potassium supplementation may be required.

Hyaluronidase, Recombinant; Immune Globulin: (Minor) Corticosteroids (e.g., cortisone, corticotropin, ACTH), when given in large systemic doses, may render tissues partially resistant to the action of hyaluronidase. Patients receiving these medications may require larger amounts of hyaluronidase for equivalent dispersing effect.

Hydralazine; Hydrochlorothiazide, HCTZ: (Moderate) Additive hypokalemia may occur when non-potassium sparing diuretics, including thiazide diuretics, are coadministered with other drugs with a significant risk of hypokalemia, such as corticosteroids. Monitoring serum potassium levels and cardiac function is advised, and potassium supplementation may be required.

Hydralazine; HCTZ: (Moderate) Additive hypokalemia may occur when non-potassium sparing diuretics, including thiazide diuretics, are coadministered with other drugs with a significant risk of hypokalemia, such as corticosteroids. Monitoring serum potassium levels and cardiac function is advised, and potassium supplementation may be required.

Heparin: (Moderate) Concomitant use of systemic sodium chloride, especially at high doses, and corticosteroids may result in sodium and fluid retention. Assess sodium chloride intake from all sources, including intake from sodium-containing intravenous fluids and antibiotic admixtures. Carefully monitor sodium concentrations and fluid status if sodium-containing drugs and corticosteroids must be used together.
Hydrochlorothiazide, HCTZ; Losartan: (Moderate) Additive hypokalemia may occur when non-potassium sparing diuretics, including thiazide diuretics, are coadministered with other drugs with a significant risk of hypokalemia, such as corticosteroids. Monitoring serum potassium levels and cardiac function is advised, and potassium supplementation may be required.

Hydrochlorothiazide, HCTZ; Methylprednisolone: (Moderate) Additive hypokalemia may occur when non-potassium sparing diuretics, including thiazide diuretics, are coadministered with other drugs with a significant risk of hypokalemia, such as corticosteroids. Monitoring serum potassium levels and cardiac function is advised, and potassium supplementation may be required.

Hydrochlorothiazide, HCTZ; Metoprolol: (Moderate) Additive hypokalemia may occur when non-potassium sparing diuretics, including thiazide diuretics, are coadministered with other drugs with a significant risk of hypokalemia, such as corticosteroids. Monitoring serum potassium levels and cardiac function is advised, and potassium supplementation may be required.

Hydrochlorothiazide, HCTZ; Moxifloxacin: (Moderate) Additive hypokalemia may occur when non-potassium sparing diuretics, including thiazide diuretics, are coadministered with other drugs with a significant risk of hypokalemia, such as corticosteroids. Monitoring serum potassium levels and cardiac function is advised, and potassium supplementation may be required.

Hydrochlorothiazide, HCTZ; Olmesartan: (Moderate) Additive hypokalemia may occur when non-potassium sparing diuretics, including thiazide diuretics, are coadministered with other drugs with a significant risk of hypokalemia, such as corticosteroids. Monitoring serum potassium levels and cardiac function is advised, and potassium supplementation may be required.

Hydrochlorothiazide, HCTZ; Propranolol: (Moderate) Additive hypokalemia may occur when non-potassium sparing diuretics, including thiazide diuretics, are coadministered with other drugs with a significant risk of hypokalemia, such as corticosteroids. Monitoring serum potassium levels and cardiac function is advised, and potassium supplementation may be required.

Hydrochlorothiazide, HCTZ; Telmisartan: (Moderate) Additive hypokalemia may occur when non-potassium sparing diuretics, including thiazide diuretics, are coadministered with other drugs with a significant risk of hypokalemia, such as corticosteroids. Monitoring serum potassium levels and cardiac function is advised, and potassium supplementation may be required.

Hydrochlorothiazide, HCTZ; Triamterene: (Moderate) Additive hypokalemia may occur when non-potassium sparing diuretics, including thiazide diuretics, are coadministered with other drugs with a significant risk of hypokalemia, such as corticosteroids. Monitoring serum potassium levels and cardiac function is advised, and potassium supplementation may be required.

Hydrochlorothiazide, HCTZ; Valsartan: (Moderate) Additive hypokalemia may occur when non-potassium sparing diuretics, including thiazide diuretics, are coadministered with other drugs with a significant risk of hypokalemia, such as corticosteroids. Monitoring serum potassium levels and cardiac function is advised, and potassium supplementation may be required.

Hydrocodeine; Phenylephrine: (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.

Hydrocortisone: Because systemic corticosteroids exhibit immunosuppressive effects when given in high doses and/or for extended periods, additive effects may be seen with other immunosuppressives or antineoplastic agents.

Hyoscyamine; Methenamine; Methylen Blue; Phenyli Salicylate; Sodium Biphosphate: (Moderate) Salicylates or NSAIDs should be used cautiously in patients receiving corticosteroids. While there is controversy regarding the ulcerogenic potential of corticosteroids alone, concomitant administration of corticosteroids with aspirin may increase the GI toxicity of aspirin and other non-acetylated salicylates. With corticosteroids and aspirin given concomitantly, an increased incidence of GI side effects such as ulceration and bleeding, in addition to a possible additive effect on tissue damage, has been noted. Corticosteroids may increase the risk of adverse GI events due to NSAIDs. Although some patients may need to be given corticosteroids and NSAIDs concomitantly, which can be done successfully for short periods of time without sequelae, prolonged coadministration should be avoided. (Moderate) Use sodium phosphate cautiously with corticosteroids, especially mineralocorticoids or corticotropin, ACTH, as concurrent use can cause hypernatremia.

Hydroxyurea: (Moderate) Use sodium phosphate cautiously with corticosteroids, especially mineralocorticoids or corticotropin, ACTH, as concurrent use can cause hypernatremia. (Minor) Because systemically administered corticosteroids exhibit immunosuppressive effects when given in high doses and/or for extended periods, additive effects may be seen with other immunosuppressives or antineoplastic agents.

Ibritumomab Tiuxetan: (Minor) Because systemically administered corticosteroids exhibit immunosuppressive effects when given in high doses and/or for extended periods, additive effects may be seen with other immunosuppressives or antineoplastic agents.

Indapamide: (Moderate) Additive hypokalemia may occur when indapamide is coadministered with other drugs with a significant risk of hypokalemia such as systemic corticosteroids. Coadministration with caution and careful monitoring.

Insulin Degludec; Liraglutide: (Moderate) Monitor patients receiving antidiabetic agents closely for worsening glycemic control when corticosteroids are instituted and for signs of hypoglycemia when corticosteroids are discontinued. Systemic and inhaled corticosteroids are known to increase blood glucose and worsen glycemic control in patients taking antidiabetic agents. The main risk factors for impaired glucose tolerance due to corticosteroids are the dose of steroid and duration of treatment. Corticosteroids stimulate hepatic glucose production and inhibit peripheral glucose uptake into muscle and fatty tissues, producing insulin resistance. Decreased insulin production may occur in the pancreas due to a direct effect on pancreatic beta cells.

Insulin Glargin; Lixisenatide: (Moderate) Monitor patients receiving antidiabetic agents closely for worsening glycemic control when corticosteroids are instituted and for signs of hypoglycemia when corticosteroids are discontinued. Systemic and inhaled corticosteroids are known to increase blood glucose and worsen glycemic control in patients taking antidiabetic agents. The main risk factors for impaired glucose tolerance due to corticosteroids are the dose of steroid and duration of treatment. Corticosteroids stimulate hepatic glucose production and inhibit peripheral glucose uptake into muscle and fatty tissues, producing insulin resistance. Decreased insulin production may occur in the pancreas due to a direct effect on pancreatic beta cells.

Insulins: (Moderate) Monitor patients receiving insulin closely for worsening glycemic control when corticosteroids are instituted and for signs of hypoglycemia when corticosteroids are discontinued. Systemic and inhaled corticosteroids are known to increase blood glucose and worsen glycemic control in patients taking antidiabetic agents. The main risk factors for impaired glucose tolerance due to corticosteroids are the dose of steroid and duration of treatment. Corticosteroids stimulate hepatic glucose production and inhibit peripheral glucose uptake into muscle and fatty tissues, producing insulin resistance. Decreased insulin production may occur in the pancreas due to a direct effect on pancreatic beta cells.

Interferon Alfa-2a: (Minor) Because systemically administered corticosteroids exhibit immunosuppressive effects when given in high doses and/or for extended periods, additive effects may be seen with other immunosuppressives or antineoplastic agents.

Interferon Alfa-2b: (Minor) Because systemically administered corticosteroids exhibit immunosuppressive effects when given in high doses and/or for extended periods, additive effects may be seen with other immunosuppressives or antineoplastic agents.

Intranasal Influenza Vaccine: (Severe) Live virus vaccines should generally not be administered to an immunosuppressed patient. Live virus vaccines may induce the illness they are intended to prevent and are generally contraindicated for use during immunosuppressive treatment. The immune response of the immunocompromised patient to vaccines may be decreased, even despite alternate vaccination schedules or more
frequent booster doses. If immunization is necessary, choose an alternative to live vaccination, or, consider a delay or change in the immunization schedule. Practitioners should refer to the most recent CDC guidelines regarding vaccination of patients who are receiving drugs that adversely affect the immune system. Children who are receiving high doses of systemic corticosteroids (i.e., greater than or equal to 2 mg/kg prednisone orally per day) for 2 weeks or more may be vaccinated after steroid therapy has been discontinued for at least 3 months in accordance with general recommendations for the use of live-virus vaccines. The CDC has stated that discontinuation of steroids for 1 month prior to varicella virus vaccine live virus should be sufficient. Budesonide may affect the immunogenicity of live vaccines. An open-label study examined the immunogenicity to varicella vaccine in 243 pediatric asthma patients who were treated with budesonide inhalation suspension 0.251 mg daily (n = 151) or non-corticosteroid asthma therapy (n = 92). The percentage of patients developing a seroprotective antibody titer of at least 5 (gpELISA value) in response to the vaccination was slightly lower in patients treated with budesonide compared to patients treated with non-corticosteroid asthma therapy (85% vs. 90%). Even though no patient treated with budesonide inhalation suspension developed chicken pox because of vaccination, live-virus vaccines should not be given to individuals who are considered to be immunocompromised until more information is available.

Isoprotenerol: (Moderate) The risk of cardiac toxicity with isoprotenerol in asthma patients appears to be increased with the coadministration of corticosteroids. Intravenous infusions of isoprotenerol in refractory asthmatic children at rates of 0.05 to 2.7 mg/kg/min have caused clinical deterioration, ventricular infarction (necrosis), congestive heart failure and death.

Isotretinoin: (Minor) Both isotretinoin and corticosteroids can cause osteoporosis during chronic use. Patients receiving systemic corticosteroids should receive isoretinoin therapy with caution.

L-Asparaginase Escherichia coli: (Moderate) Concomitant use of L-asparaginase with corticosteroids can result in additive hyperglycemia. L-Asparaginase transiently inhibits insulin production contributing to hyperglycemia seen during concurrent corticosteroid therapy. Insulin therapy may be required in some cases. Administration of L-asparaginase after rather than before corticosteroids reportedly has produced fewer hypersensitivity reactions.

Levetiracetam: (Moderate) Concomitant use of systemic sodium chloride, especially at high doses, and corticosteroids may result in sodium and fluid retention. Assess sodium chloride intake from all sources, including intake from sodium-containing intravenous fluids and antibiotic admixtures. Carefully monitor sodium concentrations and fluid status if sodium-containing drugs and corticosteroids must be used together.

Lenvemethyll: (Major) Caution is advised when using levetiracetam in combination with other agents, such as corticosteroids, that may lead to electrolyte abnormalities, especially hypokalemia or hypomagnesemia.

Linaclotide: Metformin: (Moderate) Monitor patients receiving antidiabetic agents closely for worsening glycemic control when corticosteroids are instilled and for signs of hypoglycemia when corticosteroids are discontinued. Systemic and inhaled corticosteroids are known to increase blood glucose and worsen glycemic control in asthmatic patients. The main risk factors for impaired glucose tolerance when corticosteroids are the dose of steroid and duration of treatment. Corticosteroids stimulate hepatic glucose production and inhibit peripheral glucose uptake into muscle and fatty tissues, producing insulin resistance. Decreased insulin production may occur in the pancreas due to a direct effect on pancreatic beta cells.

Linagliptin: (Moderate) Monitor patients receiving antidiabetic agents closely for worsening glycemic control when corticosteroids are instilled and for signs of hypoglycemia when corticosteroids are discontinued. Systemic and inhaled corticosteroids are known to increase blood glucose and worsen glycemic control in patients taking antidiabetic agents. The main risk factors for impaired glucose tolerance due to corticosteroids are the dose of steroid and duration of treatment. Corticosteroids stimulate hepatic glucose production and inhibit peripheral glucose uptake into muscle and fatty tissues, producing insulin resistance. Decreased insulin production may occur in the pancreas due to a direct effect on pancreatic beta cells.

Lisdexametason: (Minor) The amphetamines may interfere with laboratory tests for the determination of corticosteroids. Plasma cortisol concentrations may be increased, especially during evening hours. Amphetamines may also interfere with urinary steroid determinations.

Live Vaccines: (Severe) Live virus vaccines should generally not be administered to an immunosuppressed patient. Live virus vaccines may induce the illness they are intended to prevent and are generally contraindicated for use during immunosuppressive treatment. The immune response of the immunocompromised patient is to vaccine is usually decreased despite alternate vaccination schedules or more frequent booster doses. If immunization is necessary, choose an alternative to live vaccination, or, consider a delay or change in the immunization schedule. Practitioners should refer to the most recent CDC guidelines regarding vaccination of patients who are receiving drugs that adversely affect the immune system.

Children who are receiving high doses of systemic corticosteroids (i.e., greater than or equal to 2 mg/kg prednisone orally per day) for 2 weeks or more may be vaccinated after steroid therapy has been discontinued for at least 3 months in accordance with general recommendations for the use of live-virus vaccines. The CDC has stated that discontinuation of steroids for 1 month prior to varicella virus vaccine live virus should be sufficient. Budesonide may affect the immunogenicity of live vaccines. An open-label study examined the immunogenicity of varicella vaccine in 243 pediatric asthma patients who were treated with

Macimorelin: (Moderate) Avoid use of macimorelin with drugs that directly affect pituitary growth hormone secretion, such as corticosteroids.

Magnesium Salicylate: Use of these medications together may impact the accuracy of the macimorelin growth hormone test.

Loop diuretics: (Severe) Loop diuretics may increase the risk of cardiac toxicity with isoprotenerol in asthma patients. Also, corticosteroids may accentuate the electrolyte loss associated with diuretic therapy resulting in hypokalemia.

Macromel: (Major) Avoid use of macromel in patients receiving corticosteroids concomitantly.

Magnesium Salicylate: (Moderate) Salicylates or Magnesium Salicylate should be used with caution in patients receiving corticosteroids. While there is controversy regarding the ulcerogenic potential of corticosteroids alone, concomitant administration of corticosteroids with aspirin may increase the GI toxicity of aspirin and other non-acylated salicylates. Withdrawal of corticosteroids can result in increased plasma concentrations of salicylate and possibly toxicity. Concomitant use of corticosteroids may increase the risk of adverse GI events due to NSAIDs. Although some patients may need to continue corticosteroids and NSAIDs concomitantly, which can be done successfully for short periods of time without sequelae, prolonged coadministration should be avoided.

Mannitol: (Moderate) Corticosteroids may accentuate the electrolyte loss associated with diuretic therapy resulting in hypokalemia. Also, corticosteroids may cause calcium loss and sodium and fluid retention. Mannitol itself can cause hypernatremia. Close monitoring of electrolytes should occur in patients receiving these drugs concomitantly.

Macromel: (Major) Avoid use of macromel in patients receiving corticosteroids concomitantly.

Mead Virus; Mumps Virus; Rubella Virus; Varicella Virus Vaccine, Live: (Severe) Live virus vaccines should generally not be administered to an immunosuppressed patient. Live virus vaccines may induce the illness they are intended to prevent and are generally contraindicated for use during immunosuppressive treatment. The immune response of the immunocompromised patient to vaccines may be decreased, even despite alternate vaccination schedules or more frequent booster doses. If immunization is necessary, choose an alternative to live vaccination, or, consider a delay or change in the immunization schedule. Practitioners should refer to the most recent CDC guidelines regarding vaccination of patients who are receiving drugs that adversely affect the immune system. Children who are receiving high doses of systemic corticosteroids (i.e., greater than or equal to 2 mg/kg prednisone orally per day) for 2 weeks or more may be vaccinated after steroid therapy has been discontinued for at least 3 months in accordance with general recommendations for the use of live-virus vaccines. The CDC has stated that discontinuation of steroids for 1 month prior to varicella virus vaccine live vaccine administration may be sufficient. Budesonide may affect the immunogenicity of live vaccines. An open-label study examined the immunogenicity to varicella vaccine in 243 pediatric asthma patients who were treated with
**Mecasermin rinfabate:** (Moderate) Additional monitoring may be required when coadministering systemic or inhaled corticosteroids and mecasermin, recombinant, rh-IGF-1. In animal studies, corticosteroids impair the growth-stimulating effects of growth hormone (GH) through interference with the physiological stimulation of epiphyseal chondrocyte proliferation exalted by GH and IGF-1. Dexamethasone administration on long bone in vitro results in a decrease of local synthesis of IGF-1. Similar growth-stimulating effects are expected in humans. If systemic or inhaled glucocorticoid therapy is required, the steroid dose should be carefully adjusted and growth rate monitored.

**Mecasermin, Recombinant, rh-IGF-1:** (Moderate) Additional monitoring may be required when coadministering systemic or inhaled corticosteroids and mecasermin and mecasermin, recombinant, rh-IGF-1. In animal studies, corticosteroids impair the growth-stimulating effects of growth hormone (GH) through interference with the physiological stimulation of epiphyseal chondrocyte proliferation exalted by GH and IGF-1. Dexamethasone administration on long bone in vitro results in a decrease of local synthesis of IGF-1. Similar growth-stimulating effects are expected in humans. If systemic or inhaled glucocorticoid therapy is required, the steroid dose should be carefully adjusted and growth rate monitored.

**Methenamine; Sodium Acid Phosphate; Methylene Blue; Hyoscyamine:** (Minor) Because systemically administered corticosteroids exhibit immunosuppressive effects when given in high doses and/or for extended periods, additive effects may be seen with other immunosuppressives or antineoplastic agents. Methenamine, sodium acid phosphate, methylene blue, and hyoscyamine may be used concurrently with corticosteroids, but closer monitoring of blood pressure and potassium levels may be necessary.

**Methyclothiazide:** (Moderate) Corticosteroids may increase the risk of hypokalemia if used concurrently with methyclothiazide. Hypokalemia may be especially severe with prolonged use of corticotropin, ACTH. Monitor serum potassium levels to determine the need for potassium supplementation and/or alteration in drug therapy. The chronic use of corticosteroids may augment calcium excretion with methyclothiazide leading to increased risk for hypocalcemia and/or osteoporosis.

**Methenamine; Sodium Acid Phosphate:** (Moderate) Use sodium phosphate cautiously with corticosteroids, especially mineralocorticoids or corticosteroids used concurrently with cause hypernatremia.

**Methenamine; Sodium Acid Phosphate; Methylene Blue; Hyoscyamine:** (Moderate) Use sodium phosphate cautiously with corticosteroids, especially mineralocorticoids or corticosteroids, as concurrent use can cause hypernatremia.

**Metyrosine:** (Minor) Because systemically administered corticosteroids exhibit immunosuppressive effects when given in high doses and/or for extended periods, additive effects may be seen with other immunosuppressives or antineoplastic agents. Metyrosine may be used concurrently with corticosteroids, but closer monitoring of blood pressure and potassium levels may be necessary.
administered with other drugs with a significant risk of hyponatremia, such as corticosteroids. Monitoring serum potassium levels and cardiac function is advised, and potassium supplementation may be required.

Metolazone: (Moderate) Additive hyponatremia may occur when non-potassium sparing diuretics, including thiazide diuretics, are coadministered with other drugs with a significant risk of hyponatremia, such as corticosteroids. Monitoring serum potassium levels and cardiac function is advised, and potassium supplementation may be required.

Mifepristone: (Major) Because systemically administered corticosteroids exhibit immunosuppressive effects when given in high doses and/or for extended periods, additive effects may be seen with other immunosuppressives or antineoplastic agents.

Mivacurium: (Moderate) Caution and close monitoring are advised if corticosteroids and neuromuscular blockers are used together, particularly for long periods, due to enhanced neuromuscular blocking effects. In such patients, a peripheral nerve stimulator may be of value in monitoring the response. Concurrent use may increase the risk of acute myopathy. This acute myopathy is generalized, may involve ocular and respiratory muscles, and may result in quadriparesis. Elevation of creatine kinase may occur. Clinical improvement or recovery after stopping corticosteroids may require weeks to years.

Mifepristone: (Moderate) Concomitant use of systemic sodium chloride, especially at high doses, and corticosteroids may result in sodium and fluid retention. Assess sodium chloride intake from all sources, including intake from sodium-containing intravenous fluids and antibiotic admixtures. Carefully monitor sodium concentrations and fluid status if sodium-containing drugs and corticosteroids must be used together.

Muromonab-CD3: (Major) Because systemically administered corticosteroids exhibit immunosuppressive effects when given in high doses and/or for extended periods, additive effects may be seen with other immunosuppressives or antineoplastic agents. While therapy is designed to take advantage of these interactions, patients may be at risk for excessive sedation resulting in an increased risk of serious infections. Close clinical monitoring is advised with concurrent use; in the presence of serious infections, continuation of the corticosteroid or immunosuppressive agent may be necessary but should be accompanied by appropriate antimicrobial therapies as indicated.

Natalizumab: (Major) Ordinarily, patients receiving chronic immunosuppressant therapy should not be treated with natalizumab. Treatment recommended for combined corticosteroid and therapy for natalizumab may be initiated at low doses and with close clinical monitoring. The dosage should be increased gradually as tolerated, with continued carefully monitoring of the patient's clinical status.

Neuromuscular blockers: (Moderate) Caution and close monitoring are advised if corticosteroids and neuromuscular blockers are used together, particularly for long periods, due to enhanced neuromuscular blocking effects. In such patients, a peripheral nerve stimulator may be of value in monitoring the response. Concurrent use may increase the risk of acute myopathy. This acute myopathy is generalized, may involve ocular and respiratory muscles, and may result in quadriparesis. Elevation of creatine kinase may occur. Clinical improvement or recovery after stopping corticosteroids may require weeks to years.

Nonsteroidal antiinflammatory drugs: (Moderate) Although some patients may need to be given corticosteroids and NSAIDs concurrently, which may increase the success of the corticosteroids. Short-term use of corticosteroids should be avoided. Concomitant use of corticosteroids appears to increase the risk of adverse GI events due to NSAIDs. Corticosteroids can have profound effects on sodium-potassium balance; NSAIDs also can affect sodium and fluid balance. Monitor serum potassium concentrations; potassium supplementation may be necessary. In addition, NSAIDs may mask fever, pain, swelling and other signs and symptoms of an infection; use NSAIDs with caution in patients receiving immunosuppressant dosages of corticosteroids. The Beers criteria recommends that this drug combination be avoided in elderly adults. Monitoring serum potassium cannot be avoided, provide gastrointestinal care, and provide hydration. Carefully monitor serum sodium concentrations and fluid status if sodium-containing drugs and corticosteroids must be used together.

Ondansetron: (Moderate) Concomitant use of systemic sodium chloride, especially at high doses, and corticosteroids may result in sodium and fluid retention. Assess sodium chloride intake from all sources, including intake from sodium-containing intravenous fluids and antibiotic admixtures. Carefully monitor serum sodium concentrations and fluid status if sodium-containing drugs and corticosteroids must be used together.

Oxytocin (Human) Concomitant use of oxytetracycline with corticosteroids or corticotropin, ACTH may cause increased edema. Manage edema with diuretic and/or digitalis therapy.

Pancuronium: (Moderate) Caution and close monitoring are advised if corticosteroids and neuromuscular blockers are used together, particularly for long periods, due to enhanced neuromuscular blocking effects. In such patients, a peripheral nerve stimulator may be of value in monitoring the response. Concurrent use may increase the risk of acute myopathy. This acute myopathy is generalized, may involve ocular and respiratory muscles, and may result in quadriparesis. Elevation of creatine kinase may occur. Clinical improvement or recovery after stopping corticosteroids may require weeks to years.

Pegasparaginase: (Moderate) Concomitant use of pegaspargase with corticosteroids can result in additive hyperglycemia. Insulin therapy may be required in some cases.

Penicillamine: (Major) Agents such as immunosuppressives have adverse reactions similar to those of penicillamine. Concomitant use of penicillamine with these agents is contraindicated because of the increased risk of developing severe hematologic and renal toxicity.

Phenylephrine: (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.

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Photonsensitizing effects: (Minor) Corticosteroids administered systemically prior to or concomitantly with photosensitizing agents may decrease the efficacy of photodynamic therapy.

Phystosugmine: (Minor) Corticosteroids may interact with cholinesterase inhibitors, occasionally causing severe muscle weakness in patients with myasthenia gravis. Glucocorticoids are occasionally used therapeutically, however, in the treatment of some patients with myasthenia gravis. In such patients, it is recommended that corticosteroid therapy be initiated at low doses and increased at close clinical monitoring. The dosage should be increased gradually as tolerated, with continued careful monitoring of the patient’s clinical status.

Pimozide: (Moderate) According to the manufacturer of pimozide, the drug should not be coadministered with drugs known to cause electrolyte imbalances, such as high-dose, systemic corticosteroid therapy. Pimozide is associated with a well-established risk of QT prolongation and torsade de points (TdP), and electrolyte imbalances (e.g., hypokalemia, hypocalcemia, hypomagnesemia) may increase the risk of life-threatening arrhythmias. Pimozide is contraindicated in patients with known hypokalemia or hypomagnesemia. Topical corticosteroids are less likely to interact.

Potassium: (Moderate) Corticosteroids, especially at high doses, may increase potassium loss, such as systemic corticosteroids.

Potassium-sparing diuretics: (Minor) The manufacturer of spironolactone lists corticosteroids as a potential drug that interacts with spironolactone. Intensified electrolyte depletion, particularly hypokalemia, may occur. However, potassium-sparing diuretics such as spironolactone do not induce hypokalemia. In fact, hypokalemia is one of the indications for potassium-sparing diuretic therapy. Therefore, drugs that induce hypokalemia, such as corticosteroids, could counter the hyperkalemic effects of potassium-sparing diuretics.

Pramlintide: (Moderate) Monitor patients receiving antidiabetic agents closely for worsening glycemic control when corticosteroids are instituted and for signs of hypoglycemia when corticosteroids are discontinued. Systemic and inhaled corticosteroids are known to increase blood glucose and worsen glycemic control in patients taking antidiabetic agents. The main risk factors for impaired glucose tolerance due to corticosteroids are the dose of steroid and duration of treatment. Corticosteroids stimulate hepatic glucose production and inhibit peripheral glucose uptake into muscles and fatty tissues, producing insulin resistance. Decreased insulin production may occur in the pancreas due to a direct effect on pancreatic beta cells.

Prasterone, Dehydroepiandrosterone, DHEA (Dietary Supplements): (Moderate) Corticosteroids blunt the adrenal secretion of endogenous DHEA and DHEAS, resulting in reduced DHEA and DHEAS serum concentrations.

Prasterone, Dehydroepiandrosterone, DHEA (FDA-approved): (Moderate) Corticosteroids blunt the adrenal secretion of endogenous DHEA and DHEAS, resulting in reduced DHEA and DHEAS serum concentrations.

Propranolol: (Moderate) Patients receiving corticosteroids during propranolol therapy may be at increased risk of hypoglycemia due to the loss of counter-regulatory cortisol response. This effect may be more pronounced in infants and young children. If concurrent use is necessary, carefully monitor vital signs and blood glucose concentrations as clinically indicated.

Purine analogs: (Minor) Concurrent use of purine analogs with other agents which cause bone marrow or immune suppression such as other antineoplastic agents or immunosuppressives may result in additive effects.

Pyridostigmine: (Minor) Corticosteroids may interact with cholinesterase inhibitors including ambenonium, neostigmine, and pyridostigmine, occasionally causing severe muscle weakness in patients with myasthenia gravis. Glucocorticoids are occasionally used therapeutically, however, in the treatment of some patients with myasthenia gravis. In such patients, it is recommended that corticosteroid therapy be initiated at low doses and increased at close clinical monitoring. The dosage should be increased gradually as tolerated, with continued careful monitoring of the patient’s clinical status.

Quetiapine: (Major) QT prolongation has occurred during concurrent use of quetiapine and medications known to cause electrolyte imbalance. Therefore, caution is advisable during concurrent use of quetiapine and corticosteroids.

Rapacuronium: (Moderate) Caution and close monitoring are advised if corticosteroids and neuromuscular blockers are used together, particularly for long periods, due to enhanced neuromuscular blocking effects. In such patients, a peripheral nerve stimulator may be of value in monitoring the response. Concurrent use may increase the risk of acute myopathy. This acute myopathy is generalized, may involve ocular and respiratory muscles, and may result in quadriparesis. Elevation of creatine kinase may occur. Clinical improvement or recovery after stopping corticosteroids may require weeks to years.

Repaglinide: (Moderate) Monitor patients receiving antidiabetic agents closely for worsening glycemic control when corticosteroids are instituted and for signs of hypoglycemia when corticosteroids are discontinued. Systemic and inhaled corticosteroids are known to increase blood glucose and worsen glycemic control in patients taking antidiabetic agents. The main risk factors for impaired glucose tolerance due to corticosteroids are the dose of steroid and duration of treatment. Corticosteroids stimulate hepatic glucose production and inhibit peripheral glucose uptake into muscles and fatty tissues, producing insulin resistance. Decreased insulin production may occur in the pancreas due to a direct effect on pancreatic beta cells.

Ritodrine: (Moderate) Ritodrine has caused maternal pulmonary edema, which appears more often in patients treated concomitantly with corticosteroids. Patients so treated should be closely monitored in the hospital.

Rituximab: (Moderate) Rituximab and corticosteroids are commonly used together; however, monitor the patient for immunosuppression and signs and symptoms of infection during combined chronic therapy.

Rituximab; Hylauronidase: (Moderate) Rituximab and corticosteroids are commonly used together; however, monitor the patient for immunosuppression and signs and symptoms of infection during combined chronic therapy. (Minor) Corticosteroids (e.g., cortisone, corticotropin, ACTH), when given in large systemic doses, may render tissues partially resistant to the action of hyaluronidase. Patients receiving these medications require larger amounts of hyaluronidase for equivalent dispersing effect.

Rocuronium: (Moderate) Caution and close monitoring are advised if corticosteroids and neuromuscular blockers are used together, particularly for long periods, due to enhanced neuromuscular blocking effects. In such patients, a peripheral nerve stimulator may be of value in monitoring the response. Concurrent use may increase the risk of acute myopathy. This acute myopathy is generalized, may involve ocular and respiratory muscles, and may result in quadriparesis. Elevation of creatine kinase may occur. Clinical improvement or recovery after stopping corticosteroids may require weeks to years.

Rotavirus Vaccine: (Severe) Live virus vaccines should generally not be administered to an immunosuppressed patient. Live virus vaccines may induce the illness they are intended to prevent and are generally contraindicated for use during immunosuppressive treatment. The immune response to the vaccine in immunocompromised patients may be decreased, even despite alternate vaccination schedules or more
frequent booster doses. If immunization is necessary, choose an alternative to live vaccination, or, consider a delay or change in the immunization schedule. Practitioners should refer to the most recent CDC guidelines regarding vaccination of patients who are receiving drugs that adversely affect the immune system. Children who are receiving high doses of systemic corticosteroids (i.e., greater than or equal to 2 mg/kg prednisone orally per day) for 2 weeks or more may be vaccinated after steroid therapy has been discontinued for at least 3 months in accordance with general recommendations for the use of live-virus vaccines. The CDC has stated that discontinuation of steroids for 1 month prior to varicella virus vaccine live administration may be sufficient. Budesonide may affect the immunogenicity of live vaccines. An open-label study examined the immune responsiveness to varicella vaccine in 243 pediatric asthma patients who were treated with budesonide inhalation suspension 0.251 mg daily (n = 151) or non-corticosteroid asthma therapy (n = 92). The percentage of patients developing a seroprotective antibody titer of at least 5 (gpELISA value) in response to the vaccination was slightly lower in patients treated with budesonide compared to patients treated with non-corticosteroid asthma therapy (85% vs. 90%). Even though no patient treated with budesonide inhalation suspension developed chicken pox because of vaccination, live-virus vaccines should not be given to individuals who are considered to be immunocompromised until more information is available.

Salicylates: (Moderate) Salicylates or NSAIDs should be used cautiously in patients receiving corticosteroids. While there is controversy regarding the ulcerogenic potential of corticosteroids alone, concomitant administration of corticosteroids with aspirin may increase the GI toxicity of aspirin and other non-acetylated salicylates. Withdrawal of corticosteroids can result in increased plasma concentrations of salicylate and possible toxicity. Concomitant use of corticosteroids may increase the risk of adverse GI events due to NSAIDs. Although some patients may need to be given corticosteroids and NSAIDs concomitantly, which can be done successfully for short periods of time without sequelae, prolonged coadministration should be avoided.

Salsalate: (Moderate) Salicylates or NSAIDs should be used cautiously in patients receiving corticosteroids. While there is controversy regarding the ulcerogenic potential of corticosteroids alone, concomitant administration of corticosteroids with aspirin may increase the GI toxicity of aspirin and other non-acetylated salicylates. Withdrawal of corticosteroids can result in increased plasma concentrations of salicylate and possible toxicity. Concomitant use of corticosteroids may increase the risk of adverse GI events due to NSAIDs. Although some patients may need to be given corticosteroids and NSAIDs concomitantly, which can be done successfully for short periods of time without sequelae, prolonged coadministration should be avoided.

Sargramostim, GM-CSF: (Major) Avoid the concomitant use of sargramostim and systemic corticosteroid agents due to the risk of additive myeloproliferative effects. If coadministration of these drugs is required, frequently monitor patients for clinical and laboratory signs of excess myeloproliferative effects (e.g., leukocytosis). Sargramostim is a recombinant human granulocyte-macrophage colony-stimulating factor that works by promoting proliferation and differentiation of hematopoietic progenitor cells.

Selenium: (Moderate) Monitor patients receiving antidiabetic agents for worsening glycemic control when corticosteroids are instituted and for signs of hypoglycemia when corticosteroids are discontinued. Systemic and inhaled corticosteroids are known to increase blood glucose and worsen glycemic control in patients taking antidiabetic agents. The main risk factors for impaired glucose tolerance due to corticosteroids are the dose of steroid and duration of treatment. Corticosteroids stimulate hepatic glucose production and inhibit peripheral glucose uptake into muscle and fatty tissues, producing insulin resistance. Decreased insulin production may occur in the pancreas due to a direct effect on pancreatic beta cells.

SGLT2 Inhibitors: (Moderate) Monitor patients receiving antidiabetic agents closely for worsening glycemic control when corticosteroids are instituted and for signs of hypoglycemia when corticosteroids are discontinued. Systemic and inhaled corticosteroids are known to increase blood glucose and worsen glycemic control in patients taking antidiabetic agents. The main risk factors for impaired glucose tolerance due to corticosteroids are the dose of steroid and duration of treatment. Corticosteroids stimulate hepatic glucose production and inhibit peripheral glucose uptake into muscle and fatty tissues, producing insulin resistance. Decreased insulin production may occur in the pancreas due to a direct effect on pancreatic beta cells.

Smallpox Vaccine, Vaccinia Vaccine: (Severe) Live virus vaccines should generally not be administered to an immunosuppressed patient. Live virus vaccines may induce the illness they are intended to prevent and are generally contraindicated for use during immunosuppressive treatment. The potential benefit of the vaccine must be weighed against the risk of the immunocompromised patient to vaccines may be decreased during alternate vaccination schedules or more frequent booster doses. If immunization is necessary, choose an alternative to live vaccination, or, consider a delay or change in the immunization schedule. Practitioners should refer to the most recent CDC guidelines regarding vaccination of patients who are receiving drugs that adversely affect the immune system. Children who are receiving high doses of systemic corticosteroids (i.e., greater than or equal to 2 mg/kg prednisone orally per day) for 2 weeks or more may be vaccinated at least 3 months after steroids have been discontinued in accordance with general recommendations for the use of live-virus vaccines. The CDC has stated that discontinuation of steroids for 1 month prior to varicella virus vaccine live administration may be sufficient. Budesonide may affect the immunogenicity of live vaccines. An open-label study examined the immune responsiveness to varicella vaccine in 243 pediatric asthma patients who were treated with budesonide inhalation suspension 0.251 mg daily (n = 151) or non-corticosteroid asthma therapy (n = 92). The percentage of patients developing a seroprotective antibody titer of at least 5 (gpELISA value) in response to the vaccination was slightly lower in patients treated with budesonide compared to patients treated with non-corticosteroid asthma therapy (85% vs. 90%). Even though no patient treated with budesonide inhalation suspension developed chicken pox because of vaccination, live-virus vaccines should not be given to individuals who are considered to be immunocompromised until more information is available.

Sodium Benzoate; Sodium Phenylacetate: (Moderate) Corticosteroids may cause protein breakdown, which could lead to elevated blood ammonia concentrations, especially in patients with an impaired ability to form urea. Corticosteroids should be used with caution in patients receiving treatment for hyperammonemia.

Sodium Chloride: (Moderate) Concomitant use of systemic sodium chloride, especially at high doses, and corticosteroids may result in sodium and fluid retention. Assess sodium chloride intake from all sources, including intake from sodium-containing intravenous fluids and antibiotic admixtures. Carefully monitor sodium concentrations and fluid status if sodium-containing drugs and corticosteroids must be used together.

Sodium Phenylbutyrate: (Moderate) The concurrent use of corticosteroids with sodium phenylbutyrate may increase plasma ammonia levels (hyperammonemia) by causing the breakdown of body protein. Patients with urea cycle disorders being treated with sodium phenylbutyrate usually should not receive regular treatment with corticosteroids.

Sodium Monohydrogen Monophosphate: Sodium Monobasic Dibasic Anhydrous: (Moderate) Use sodium phosphate cautiously with corticosteroids, especially mineralocorticoids or corticosteroid, ACTH, as concurrent use can cause hypernatremia.

Somatropin, rh-GH: (Moderate) Corticosteroids can retard bone growth and therefore, can inhibit the growth-promoting effects of somatropin. If corticosteroid therapy is required, the corticosteroid dose should be carefully adjusted.

Sucralfate: (Moderate) Caution and close monitoring are advised if corticosteroids and neuromuscular blockers are used together, particularly in patients with neuromuscular disease, due to enhanced neuromuscular blockade. A peripheral nerve stimulator may be of value in monitoring the response. Concurrent use may increase the risk of acute myopathy. This acute myopathy is generalized, may involve ocular and respiratory muscles, and may result in quadriparesis. Elevation of creatine kinase may occur. Clinical improvement or recovery after stopping corticosteroids may require weeks to months.

Sulfonamides: (Moderate) Monitor patients receiving antidiabetic agents closely for worsening glycemic control when corticosteroids are instituted and for signs of hypoglycemia when corticosteroids are discontinued. Systemic and inhaled corticosteroids are known to increase blood glucose and worsen glycemic control in patients taking antidiabetic agents. The main risk factors for impaired glucose tolerance due to corticosteroids are the dose of steroid and duration of treatment. Corticosteroids stimulate hepatic glucose production and inhibit peripheral glucose uptake into muscle and fatty tissues, producing insulin resistance. Decreased insulin production may occur in the pancreas due to a direct effect on pancreatic beta cells.

Television: (Moderate) The risk of myopathy may be increased if corticosteroids are coadministered with televinidine. Monitor patients for any signs or symptoms of unexplained muscle pain, tenderness, or weakness, particularly during periods of upward dosage titration.

Testosterone: (Moderate) Coadministration of corticosteroids and testosterone may increase the risk of edema, especially in patients with underlying hepatic disease. Corticosteroids with greater mineralocorticoid activity, such as fludrocortisone, may be more likely to cause edema. Administer these drugs in combination with caution.

Thiazide diuretics: (Moderate) Additive hypokalemia may occur when non-potassium sparing diuretics, including thiazide diuretics, are coadministered with other drugs with a significant risk of hypokalemia, such as corticosteroids. Monitoring serum potassium levels and cardiac function is advised, and potassium supplementation may be required.

Thymosin: (Moderate) Monitor patients receiving antidiabetic agents closely for worsening glycemic control when corticosteroids are instituted and for signs of hypoglycemia when corticosteroids are discontinued. Systemic and inhaled corticosteroids are known to increase blood glucose and worsen glycemic control in patients taking antidiabetic agents. The main risk factors for impaired glucose tolerance due to corticosteroids are the dose of steroid and duration of treatment. Corticosteroids stimulate hepatic glucose production and inhibit peripheral glucose uptake into muscle and fatty tissues, producing insulin resistance. Decreased insulin production may occur in the pancreas due to a direct effect on pancreatic beta cells.

Thiazide diuretics: (Moderate) Additive hypokalemia may occur when non-potassium sparing diuretics, including thiazide diuretics, are coadministered with other drugs with a significant risk of hypokalemia, such as corticosteroids. Monitoring serum potassium levels and cardiac function is advised, and potassium supplementation may be required.
instituted and for signs of hypoglycemia when corticosteroids are discontinued. Systemic and inhaled corticosteroids are known to increase blood glucose and worsen glycemic control in patients taking antidiabetic agents. The main risk factors for impaired glucose tolerance due to corticosteroids are the dose of steroid and duration of treatment. Corticosteroids stimulate hepatic glucose production and inhibit peripheral glucose uptake into muscle and fatty tissues, producing insulin resistance. Decreased insulin production may occur in the pancreas due to a direct effect on pancreatic beta cells.

Thyroid hormone levels (Moderate) The metabolism of corticosteroids is increased in hyperthyroidism and decreased in hypothyroidism. Dosage adjustments may be necessary when initiating, changing or discontinuing thyroid hormones or antithyroid agents.

Tobramycin: (Moderate) Concomitant use of systemic sodium chloride, especially at high doses, and corticosteroids may result in sodium and fluid retention. Assess sodium chloride intake from all sources, including intake from sodium-containing intravenous fluids and antibiotic admixtures. Carefully monitor sodium concentrations and fluid status if sodium-containing drugs and corticosteroids must be used together.

Tolbutamide: (Moderate) Monitor patients receiving antidiabetic agents closely for worsening glycemic control when corticosteroids are instituted and for signs of hypoglycemia when corticosteroids are discontinued. Systemic and inhaled corticosteroids are known to increase blood glucose and worsen glycemic control in patients taking antidiabetic agents. The main risk factors for impaired glucose tolerance due to corticosteroids are the dose of steroid and duration of treatment. Corticosteroids stimulate hepatic glucose production and inhibit peripheral glucose uptake into muscle and fatty tissues, producing insulin resistance. Decreased insulin production may occur in the pancreas due to a direct effect on pancreatic beta cells.

Tosotumomab: (Minor) Because systemically administered corticosteroids exhibit immunosuppressive effects when given in high doses and/or for extended periods, additive effects may be seen with other immunosuppressives or antineoplastic agents.

Tretinoin, ATRA: (Minor) Because systemically administered corticosteroids exhibit immunosuppressive effects when given in high doses and/or for extended periods, additive effects may be seen with other immunosuppressives or antineoplastic agents.

Tuberculin Purified Protein Derivative, PPD: (Mild) Immunosuppression may decrease the immunological response to tuberculin purified protein derivative, PPD. This suppressed reactivity can persist for up to 6 weeks after treatment discontinuation. Consider deferring the skin test until immunosuppressive therapy.

Tubocurarine: (Moderate) Close and careful monitoring are advised if corticosteroids and neuromuscular blockers are used together, particularly for long periods, due to enhanced neuromuscular blocking effects. In such patients, a peripheral nerve stimulator may be of value in monitoring the response. Concurrent use may increase the risk of acute myopathy. This acute myopathy is generalized, may involve ocular and respiratory muscles, and may result in quadriparesis. Elevation of creatine kinase may occur. Clinical improvement or recovery after stopping corticosteroids may take weeks to years.

Typhoid Vaccine: (Severe) Live virus vaccines should generally not be administered to an immunosuppressed patient. Live virus vaccines may induce the illness they intend to prevent and are generally contraindicated for use during immunosuppressive treatment. The immune response of the immunocompromised patient to vaccines may be decreased, even despite alternate vaccination schedules or more frequent booster doses. Discontinue corticosteroids as necessary in order to achieve or maintain a normal immune system. Children who are receiving high doses of systemic corticosteroids (i.e., greater than or equal to 2 mg/kg prednisone or prednisolone daily) for 2 weeks or more may be vaccinated after steroid therapy has been discontinued for at least 3 months in accordance with general recommendations for the use of live-virus vaccines. The CDC has stated that discontinuation of steroids for 1 month prior to varicella virus live vaccine administration may be sufficient evidence that the immune responsiveness to varicella vaccine in 243 pediatric asthmatic patients who were treated with budesonide inhalation suspension 0.251 mg daily (n = 151) or non-corticosteroid asthma therapy (n = 92). The percentage of patients developing a seroprotective antibody titer of at least 5 (gpELISA value) in response to the vaccination was slightly lower in patients treated with budesonide compared to patients treated with non-corticosteroid asthma therapy (63% vs. 70%). Even though no patient treated with budesonide or asthma suspension developed chicken pox because of vaccination, live-virus vaccines should not be given to individuals who are considered to be immunocompromised until more information is available.

Vancocymycin: (Moderate) Concomitant use of systemic sodium chloride, especially at high doses, and corticosteroids may result in sodium and fluid retention. Assess sodium chloride intake from all sources, including intake from sodium-containing intravenous fluids and antibiotic admixtures. Carefully monitor sodium concentrations and fluid status if sodium-containing drugs and corticosteroids must be used together.

Varicella-Zoster Virus Vaccine, Live: (Severe) Live virus vaccines should generally not be administered to an immunosuppressed patient. Live virus vaccines may induce the illness they intend to prevent and are generally contraindicated for use during immunosuppressive treatment. The immune response of the immunocompromised patient to vaccines may be decreased, even despite alternate vaccination schedules or more frequent booster doses. Discontinue corticosteroids as necessary in order to achieve or maintain a normal immune system. Children who are receiving high doses of systemic corticosteroids (i.e., greater than or equal to 2 mg/kg prednisone or prednisolone daily) for 2 weeks or more may be vaccinated after steroid therapy has been discontinued for at least 3 months in accordance with general recommendations for the use of live-virus vaccines. The CDC has stated that discontinuation of steroids for 1 month prior to varicella virus live vaccine administration may be sufficient evidence that the immune responsiveness to varicella vaccine in 243 pediatric asthmatic patients who were treated with budesonide inhalation suspension 0.251 mg daily (n = 151) or non-corticosteroid asthma therapy (n = 92). The percentage of patients developing a seroprotective antibody titer of at least 5 (gpELISA value) in response to the vaccination was slightly lower in patients treated with budesonide compared to patients treated with non-corticosteroid asthma therapy (63% vs. 70%). Even though no patient treated with budesonide or asthma suspension developed chicken pox because of vaccination, live-virus vaccines should not be given to individuals who are considered to be immunocompromised until more information is available.

Vaccination: (Moderate) Caution and close monitoring are advised if corticosteroids and neuromuscular blockers are used together, particularly for long periods, due to enhanced neuromuscular blocking effects. In such patients, a peripheral nerve stimulator may be of value in monitoring the response. Concurrent use may increase the risk of acute myopathy. This acute myopathy is generalized, may involve ocular and respiratory muscles, and may result in quadriparesis. Elevation of creatine kinase may occur. Clinical improvement or recovery after stopping corticosteroids may take weeks to years.

Vigabatrin: (Major) Vigabatrin should not be used with corticosteroids, which are associated with serious ophthalmic effects (e.g., retinopathy or glaucoma). The benefit of treatment clearly outweighs the risk. Use with caution.

Vinblastine: (Minor) Use caution when administering vinblastine concurrently with a CYP3A4 inducer such as dexamethasone. Vinblastine is metabolized by CYP3A4 and dexamethasone may decrease vinblastine plasma concentrations. In addition, because systemically administered corticosteroids exhibit immunosuppressive effects when given in high doses and/or for extended periods, additive effects may be seen with antineoplastic agents. While therapy is designed to take advantage of this effect, patients may be predisposed to over-immunosuppression and worsen glycemic control in patients taking antidiabetic agents. The main risk factors for impaired glucose tolerance due to corticosteroids are the dose of steroid and duration of treatment. Corticosteroids stimulate hepatic glucose production and inhibit peripheral glucose uptake into muscle and fatty tissues, producing insulin resistance. Decreased insulin production may occur in the pancreas due to a direct effect on pancreatic beta cells.

Vorinostat: (Moderate) Use vorinostat and corticosteroids together with caution; the risk of QT prolongation and arrhythmias may be increased if electrolyte abnormalities occur. Corticosteroids may cause electrolyte imbalances; hypomagnesemia, hypokalemia, or hypocalcemia and may increase the risk of QT prolongation with vorinostat. Frequently monitor serum electrolytes if concomitant use of these drugs is necessary.

Warfarin: (Moderate) The effect of corticosteroids on oral anticoagulants (e.g., warfarin) is variable. There are reports of enhanced as well as diminished effect of anticoagulants with corticosteroids; however, limited published data exist, and the mechanism of the
interaction is not well described. High-dose corticosteroids appear to pose a greater risk for increased anticoagulant effect. In addition, corticosteroids have been associated with a risk of peptic ulcer and gastrointestinal bleeding. Thus corticosteroids should be used cautiously and with appropriate clinical monitoring in patients receiving oral anticoagulants; coagulation indices (e.g., INR, etc.) should be monitored to maintain the desired anticoagulant effect. During high-dose corticosteroid administration, daily laboratory monitoring may be desirable.

**Yellow Fever Vaccine, Live:** (Severe) Live virus vaccines should generally not be administered to an immunosuppressed patient. Live virus vaccines may induce the illness they are intended to prevent and are generally contraindicated for use during immunosuppressive treatment. The immune response of the immunocompromised patient to vaccines may be decreased, even despite alternate vaccination schedules or more frequent booster doses. If immunization is necessary, choose an alternative to live vaccination, or, consider a delay or change in the immunization schedule. Practitioners should refer to the most recent CDC guidelines regarding vaccination of patients who are receiving drugs that adversely affect the immune system. Children who are receiving high doses of systemic corticosteroids (i.e., greater than or equal to 2 mg/kg prednisone orally per day) for 2 weeks or more may be vaccinated after steroid therapy has been discontinued for at least 3 months in accordance with general recommendations for the use of live-virus vaccines. The CDC has stated that discontinuation of steroids for 1 month prior to varicella virus vaccine live administration may be sufficient. Budesonide may affect the immunogenicity of live vaccines. An open-label study examined the immune responsiveness to varicella vaccine in 243 pediatric asthma patients who were treated with budesonide inhalation suspension 0.251 mg daily (n = 151) or corticosteroid asthma therapy (n = 92). The percentage of patients developing a seroprotective antibody titer of at least 5 (gpELISA value) in response to the vaccination was slightly lower in patients treated with budesonide compared to patients treated with non-corticosteroid asthma therapy (85% vs. 90%). Even though no patient treated with budesonide inhalation suspension developed chicken pox because of vaccination, live-virus vaccines should not be given to individuals who are considered to be immunocompromised until more information is available.

**Zafirlukast:** (Minor) Zafirlukast inhibits the CYP3A4 isoenzymes and should be used cautiously in patients stabilized on drugs metabolized by CYP3A4, such as corticosteroids.

**Zileuton:** (Minor) Zileuton is metabolized by the cytochrome P450 isoenzyme 3A4. Although administration of zileuton with other drugs metabolized by CYP3A4 has not been studied, zileuton may inhibit CYP3A4 isoenzymes. Zileuton could potentially compete with other CYP3A4 substrates.

**PREGNANCY AND LACTATION**

**Pregnancy**

Corticotropin, ACTH is classified as FDA pregnancy risk category C. Safe use of corticotropin during human pregnancy has not been established. Corticotropin has been shown to have an embryocidal effect and to cause fetal damage in animals. It also causes the release of cortisol and endogenous corticosteroids. Per the manufacturer, corticotropin use should be avoided during pregnancy unless the potential therapeutic benefit justifies the added risk to the fetus. Adrenocortical disease during pregnancy is relatively rare as most cases are diagnosed before a woman becomes pregnant, but ACTH stimulated normal cortisol values have been established for each trimester. Adrenal disease may cause significant maternal and fetal morbidity, so accurate and rapid diagnosis is important. The use of cosyntropin to confirm the diagnosis of adrenal insufficiency during pregnancy, when suspected, is described in the literature.

It is not known whether corticotropin, ACTH is excreted in human milk. Because many drugs are excreted in human milk and due to the potential for serious adverse reactions in nursing infants, the manufacturer states that a decision should be made whether to discontinue breast-feeding or to discontinue the drug, taking into account the importance of the drug to the mother and the indication for use. However, due to it's large molecular weight and short half-life of only 10 to 15 minutes, corticotropin, ACTH is unlikely to appear in human milk. It is unlikely that corticotropin, ACTH would be absorbed by the infant because it would probably be degraded in the infant's gastrointestinal tract. Animal data suggests an increase in breast milk cortisol levels might be expected after administration of corticotropin to a nursing mother. However, if corticotropin is required in the mother, it is not a reason to discontinue breast-feeding. Alternative therapies to consider include other corticosteroids, such as prednisone and methylprednisolone. Prednisone concentrations in breast milk are low, and no adverse effects have been reported in the breast-fed infant with maternal use of any corticosteroid during breast-feeding; prednisone is generally considered compatible to use during lactation. 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 administered drug, healthcare providers are encouraged to report the adverse effect to the FDA.

**MECHANISM OF ACTION**

Corticotropin and endogenous ACTH stimulates steroidogenesis and the release of cortisol (hydrocortisone), corticosterone, and weak androgens from the adrenal cortex. The physiologic and pharmacologic effects of corticosteroids are due primarily to the glucocorticoid cortisol, which also has some mineralocorticoid activity. Prolonged administration of large doses of corticosteroids induces hyperplasia and hypertrophy of the adrenal cortex and can lead to permanent damage to the adrenal cortex. Corticosteroids are metabolized in the liver and the metabolites are excreted in the urine. The half-life of corticosteroids is under the influence of the nervous system via the regulatory hormone released from the hypothalamus and by a negative corticosteroid feedback mechanism. Elevated plasma cortisol suppresses ACTH release. The antiinflammatory actions of corticosteroids are thought to involve phospholipase A2 inhibitory proteins, collectively called lipocortins; lipocortins control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting the release of the precursor molecule arachidonic acid. Other effects of corticosteroids include extra-adrenal effects such as binding to melanocortin receptors.

Although oral glucocorticoids do not depend on adrenal function for effectiveness, have a more predictable profile, and have easily regulated doses for patient-specific therapy, corticosteroid therapy is preferred by some clinicians in certain conditions.

The mechanism of action of corticotropin for the treatment of infantile spasms is unknown.

**PHARMACOKINETICS**

**Intramuscular Route**

Following IM injection, Corticotropin injection (CI) is rapidly absorbed, and RCI is absorbed over an 8- to 16-hour period. Maximal adrenal stimulation in adults with normal adrenal function occurs within 8 hours after infusion of 1—6 units of CI. Secretion of cortisol is greater with slow IV infusion of CI or with IM repository injection than with rapid CI infusion or with IM injection of CI.
Subcutaneous Route
Following subcutaneous injection, peak plasma concentrations of corticotropin can be attained within 3—12 hours and return to baseline within 10—25 hours.