Ranitidine
From Wikipedia, the free encyclopedia

Ranitidine (ˈrænɪtɪdɪn; trade name Zantac) is a histamine H₂-receptor antagonist that inhibits stomach acid production. It is commonly used in treatment of peptic ulcer disease and gastroesophageal reflux disease. Ranitidine is also used alongside fexofenadine and other antihistamines for the treatment of skin conditions such as hives. Ranitidine was discovered and developed by scientists at Glaxo Pharmaceuticals, now a part of GSK.

It is on the World Health Organization's List of Essential Medicines, the most important medications needed in a basic health system.[1]

### Contents

- 1 Medical uses
  - 1.1 Preparations
  - 1.2 Dosing
- 2 Contraindications
- 3 Adverse effects
  - 3.1 Central nervous system
  - 3.2 Cardiovascular
  - 3.3 Gastrointestinal
  - 3.4 Hepatic
  - 3.5 Respiratory
  - 3.6 Hematologic
  - 3.7 Integumentary
- 4 Warnings and precautions
  - 4.1 Disease-related concerns
  - 4.2 Pregnancy
  - 4.3 Lactation
  - 4.4 Children
- 5 Pharmacology
  - 5.1 Mechanism of action
  - 5.2 Pharmacokinetics
    - 5.2.1 Elderly
    - 5.2.2 Children
- 6 History
- 7 See also
- 8 References
- 9 External links

### Medical uses

- Relief of heartburn, acid indigestion, and sour stomach
- Short-term and maintenance therapy of gastric and duodenal ulcers
- Ranitidine can also be coadministered with NSAIDs to reduce the risk of ulceration. Proton-pump inhibitors (PPIs) are more effective for the prevention of NSAID-induced ulcers.[2]
- Pathologic gastrointestinal (GI) hypersecretory conditions such as Zollinger-Ellison syndrome
- Gastroesophageal reflux
- Erosive esophagitis
- Part of a multidrug regimen for *H. pylori* eradication to reduce the risk of duodenal ulcer recurrence
- Recurrent postoperative ulcer
- Upper GI bleeding
- Prevention of acid-aspiration pneumonitis during surgery: Ranitidine can be administered preoperatively to reduce the risk of aspiration pneumonia. The drug not only increases gastric pH, but also reduces the total output of gastric juice. In a 2009 meta-analysis comparing the net benefit of proton pump inhibitors and ranitidine to reduce the risk of aspiration before anesthesia, ranitidine was found to be more effective than proton pump inhibitors in reducing the volume of gastric secretions.[3] Ranitidine may have an antiemetic effect when administered preoperatively.
Preventation of stress-induced ulcers in critically ill patients

**Preparations**

Certain preparations of ranitidine are available over the counter (OTC) in various countries. In the United States, 75- and 150-mg tablets are available OTC. Zantac OTC is manufactured by Boehringer Ingelheim. In Australia, packs containing seven or 14 doses of the 150-mg tablet are available in supermarkets, small packs of 150-mg and 300-mg tablets are schedule 2 pharmacy medicines. Larger doses and pack sizes still require a prescription.

**Dosing**

For ulcer treatment, a night-time dose is especially important - as the increase in gastric/duodenal pH promotes healing overnight when the stomach and duodenum are empty. Conversely, for treating reflux, smaller and more frequent doses are more effective.

Ranitidine used to be administered long term for reflux treatment, sometimes indefinitely. However, PPIs have taken over this role. In addition, a fairly rapid tachyphylaxis can develop within 6 weeks of initiation of treatment, further limiting its potential for long-term use.

People with Zollinger–Ellison syndrome have been given very high doses without any harm.

**Contraindications**

Ranitidine is contraindicated for patients known to have hypersensitivity to the drug.

**Adverse effects**

The following adverse effects have been reported as events in clinical trials:

**Central nervous system**

Rare reports have been made of malaise, dizziness, somnolence, insomnia, and vertigo. In severely ill, elderly patients, cases of reversible mental confusion, agitation, depression, and hallucinations have been reported. Ranitidine causes fewer CNS adverse reactions and drug interactions compared to cimetidine.

**Cardiovascular**

Arrhythmias such as tachycardia, bradycardia, atrioventricular block, and premature ventricular beats have also been reported.

**Gastrointestinal**

All drugs in its class have the potential to cause vitamin B₁₂ deficiency secondary to a reduction in food-bound vitamin B₁₂ absorption. Elderly patients taking H₂ receptor antagonists are more likely to require B₁₂ supplementation than those not taking such drugs. H₂ blockers may also reduce the absorption of drugs (azole antifungals, calcium carbonate) that require an acidic stomach. In addition, multiple studies suggest the use of H₂ receptor antagonists such as raniditine may increase the risk of infectious diarrhoea, including traveller's diarrhoea and salmonellosis. Finally, by suppressing acid-mediated breakdown of proteins, ranitidine may lead to an elevated risk of developing food or drug allergies, due to undigested proteins then passing into the gastrointestinal tract, where sensitisation occurs. Patients who take these agents develop higher levels of immunoglobulin E against food, whether they had prior antibodies or not. Even months after discontinuation, an elevated level of IgE in 6% of patients was still found in this study.

**Hepatic**

Cholestatic hepatitis, liver failure, hepatitis, and jaundice have been noted, and require immediate discontinuation of the drug.

**Respiratory**

Ranitidine and other histamine H₂ receptor antagonists may increase the risk of pneumonia in hospitalized patients. They may also increase the risk of community-acquired pneumonia in adults and children.

**Hematologic**

Thrombocytopenia is a rare but known side effect. Drug-induced thrombocytopenia usually takes weeks or months to appear, but may appear within 12 hours of drug intake in a sensitized individual. Typically, the platelet count falls to 80% of normal, and thrombocytopenia may be associated with neutropenia and anemia.
Integumentary

Rash, including rare cases of erythema multiforme and rare cases of hair loss and vasculitis have been seen.[7]

Warnings and precautions

Disease-related concerns

With gastric malignancies, relief of symptoms due to the use of ranitidine does not exclude the presence of a gastric malignancy. In addition, with kidney or liver impairment, ranitidine must be used with caution. Finally, ranitidine should be avoided in patients with porphyria, as it may precipitate an attack.[20]

Pregnancy

This drug is rated pregnancy category B in the United States.

Lactation

Ranitidine enters breast milk, with peak concentrations seen at 5.5 hours after the dose in breast milk. Caution should be exercised when prescribed to nursing women.[21]

Children

In children, the use of gastric acid inhibitors has been associated with an increased risk for development of acute gastroenteritis and community-acquired pneumonia.[22] A cohort analysis including over 11,000 neonates reported an association of H2 blocker use and an increased incidence of necrotizing enterocolitis in very-low-birth-weight (VLBW) neonates.[23] In addition, about a sixfold increase in mortality, necrotizing enterocolitis, and infection (such as sepsis, pneumonia, urinary tract infection) was reported in patients receiving ranitidine in a cohort analysis of 274 VLBW neonates.[24]

Pharmacology

Mechanism of action

Ranitidine is a competitive, reversible inhibitor of the action of histamine at the histamine H2-receptors found in gastric parietal cells. This results in decreased gastric acid secretion and gastric volume, and reduced hydrogen ion concentration.

Pharmacokinetics

Absorption: Oral: 50%

Protein binding: 15%

Metabolism: N-oxide is the principal metabolite.

Half-life elimination: With normal renal function, ranitidine taken orally has a half-life of 2.5–3.0 hours. If taken intravenously, the half-life is generally 2.0–2.5 hours in a patient with normal creatinine clearance.

Excretion: The primary route of excretion is the urine. In addition, about 30% of the orally administered dose is collected in the urine as nonabsorbed drug in 24 hours.

Elderly

In the elderly population, the plasma half-life of ranitidine is prolonged to 3–4 hours secondary to decreased kidney function causing decreased clearance.[25]

Children

In general, studies of pediatric patients (aged 1 month to 16 years) have shown no significant differences in pharmacokinetic parameter values in comparison to healthy adults, when correction is made for body weight.[25]

History
Ranitidine was first prepared as AH19065 by John Bradshaw in the summer of 1977 in the Ware research laboratories of Allen & Hanburys Ltd, part of the Glaxo organization.[26][27] Its development was a response to the first in class histamine H₂-receptor antagonist, cimetidine, developed by Sir James Black at Smith, Kline and French, and launched in the United Kingdom as Tagamet in November 1976. Both companies would eventually become merged as GlaxoSmithKline following a sequence of mergers and acquisitions starting with the integration of Allen & Hanbury's Ltd and Glaxo to form Glaxo Group Research in 1979, and ultimately with the merger of Glaxo Wellcome and SmithKline Beecham in 2000. Ranitidine was the result of a rational drug-design process using what was by then a fairly refined model of the histamine H₂-receptor and quantitative structure-activity relationships.

Glaxo refined the model further by replacing the imidazole ring of cimetidine with a furan ring with a nitrogen-containing substituent, and in doing so developed ranitidine. Ranitidine was found to have a far-improved tolerability profile (i.e. fewer adverse drug reactions), longer-lasting action, and 10 times the activity of cimetidine. Ranitidine has 10% of the affinity that cimetidine has to CYP450, so it causes fewer side effects, but other H₂ blockers famotidine and nizatidine have no CYP450 significant interactions.[28]

Ranitidine was introduced in 1981 and was the world's biggest-selling prescription drug by 1987. It has since largely been superseded by the even more effective proton-pump inhibitors, with omeprazole becoming the biggest-selling drug for many years. When omeprazole and ranitidine were compared in a study of 144 people with severe inflammation and erosions or ulcers of the esophagus, 85% of those treated with omeprazole healed within eight weeks, compared to 50% of those given ranitidine. In addition, the omeprazole group reported earlier relief of heartburn symptoms.[29]

See also

- Famotidine, aka Pepcid AC, Pepcide: another popular H₂-receptor antagonist
- Nizatidine

References


External links

- Reflux Remedies: ranitidine (Zantac) (http://pharmasight.org/otc/reflux-remedies-ranitidine-zantac/)
- Zantac OTC official website (http://www.zantacotc.com/) Boehringer Ingelheim


Categories: H2 receptor antagonists | Furans | Nitroethenes | World Health Organization essential medicines | Thioethers | Amines

---

This page was last modified on 27 July 2015, at 20:40.

Text is available under the Creative Commons Attribution-ShareAlike License; additional terms may apply. By using this site, you agree to the Terms of Use and Privacy Policy. Wikipedia® is a registered trademark of the Wikimedia Foundation, Inc., a non-profit organization.