Cimetidine

Introduction: Cimetidine is in a group of drugs called histamine receptor antagonists. Cimetidine works by decreasing the amount of acid your stomach produces.

Mechanism of action: Competitive inhibition of histamine at H_2 receptors of the gastric parietal cells resulting in reduced gastric acid secretion, gastric volume and hydrogen ion concentration reduced

Pharmacology:
Onset of action: 1 hour
Duration: 6 hours
Distribution: Crosses placenta; enters breast milk
Protein binding: 20%
Metabolism: Partially hepatic
Bioavailability: 60% to 70%
Half-life elimination: Neonates: 3.6 hours; Children: 1.4 hours; Adults: Normal renal function: 2 hours
Time to peak, serum: Oral: 1-2 hours
Excretion: Primarily urine (as unchanged drug); feces (some)
Indications:

- **Short-term treatment of active duodenal ulcer.** Most patients heal within 4 weeks and there is rarely reason to use Cimetidine at full dosage for longer than 6 to 8 weeks. Concomitant antacids should be given as needed for relief of pain.
- **Maintenance therapy for duodenal ulcer patients at reduced dosage after healing of active ulcer.** Patients have been maintained on continued treatment with Cimetidine 400 mg h.s. for periods of up to 5 years.
- **Short-term treatment of active benign gastric ulcer.** There is no information concerning usefulness of treatment periods of longer than 8 weeks.
- **Erosive gastroesophageal reflux disease (GERD).** Erosive esophagitis diagnosed by endoscopy. Treatment is indicated for 12 weeks for healing of lesions and control of symptoms. The use of *Cimetidine* beyond 12 weeks has not been established.
- **Prevention of upper gastrointestinal bleeding in critically ill patients.**
- **The treatment of pathological hypersecretory conditions** (i.e., Zollinger-Ellison Syndrome, systemic mastocytosis, multiple endocrine adenomas).

Dosage:
Children: Oral, I.M., I.V.: 20-40 mg/kg/day in divided doses every 6 hours Children 12 years and Adults: Oral: Heartburn, acid indigestion, sour stomach (OTC labeling): 200 mg up to twice daily; may take 30 minutes prior to eating foods or beverages expected to cause heartburn or indigestion

Adults: Short-term treatment of active ulcers: I.M., I.V.: 300 mg every 6 hours or 37.5 mg/hour by continuous infusion; I.V. dosage should be adjusted to maintain an intragastric pH 5
Patients with an active bleed: Administer cimetidine as a continuous infusion
Dosing adjustment/interval in renal impairment:
Children and Adults:
Clcr 20-40 mL/minute: Administer every 8 hours or 75% of normal dose
Clcr 0-20 mL/minute: Administer every 12 hours or 50% of normal dose
Hemodialysis: Slightly dialyzable (5% to 20%)
Dosing adjustment/comments in hepatic impairment: Usual dose is safe in mild liver disease but use with caution and in reduced dosage in severe liver disease; increased risk of CNS toxicity in cirrhosis suggested by enhanced penetration of CNS

Side effects: Adverse effects reported in patients taking *Cimetidine* are described below by body system. Incidence figures of 1 in 100 and greater are generally derived from controlled clinical studies.
Gastrointestinal: Diarrhea (usually mild) has been reported in approximately 1 in 100 patients.
CNS: Headaches, ranging from mild to severe, have been reported. Dizziness and somnolence (usually mild) have been reported
Reversible confusional states, e.g., mental confusion, agitation, psychosis, depression, anxiety, hallucinations, disorientation, have been reported predominantly, but not exclusively, in severely ill patients.
Endocrine: Gynecomastia has been reported in patients treated for 1 month or longer.No evidence of induced endocrine dysfunction was found, and the condition remained unchanged or returned toward normal with continuing Cimetidine treatment.
Reversible impotence has been reported in patients with pathological hypersecretory disorders, e.g., Zollinger-Ellison Syndrome, receiving Cimetidine, particularly in high doses, for at least 12 months (range 12 to 79 months, mean 38 months).
Hematologic: Decreased white blood cell counts in Cimetidine -treated patients (approximately 1 per 100,000 patients), including agranulocytosis (approximately 3 per million patients), have been reported, including a few reports of recurrence on rechallenge. Thrombocytopenia (approximately 3 per million patients) and, very rarely, cases of pancytopenia or aplastic anemia have also been reported.
Hepatobiliary: Dose-related increases in serum transaminase have been reported. There have been rare reports of cholestatic or mixed cholestatic-hepatocellular effects. These were usually reversible; as in the occasional liver injury with other H_2-receptor antagonists, in exceedingly rare circumstances fatal outcomes have been reported.

Hypersensitivity: Rare cases of fever and allergic reactions including anaphylaxis and hypersensitivity vasculitis, which cleared on withdrawal of the drug, have been reported.
Renal: Rare cases of interstitial nephritis and urinary retention, which cleared on withdrawal of the drug, have been reported.
Cardiovascular: Rare cases of bradycardia, tachycardia and A-V heart block have been reported with H_2-receptor antagonists.

Musculoskeletal: There have been rare reports of reversible arthralgia and myalgia; exacerbation of joint symptoms in patients with preexisting arthritis has also been reported. Such symptoms have usually been alleviated by a reduction in cimetidine dosage.
Integumental: Mild rash and, very rarely, cases of severe generalized skin reactions including Stevens-Johnson syndrome, epidermal necrolysis, erythema multiforme, exfoliative dermatitis and generalized exfoliative erythroderma have been reported with H_2-receptor antagonists. Reversible alopecia has been reported very rarely.

Precautions:
General: Rare instances of cardiac arrhythmias and hypotension have been reported following the rapid administration of Cimetidine njection by intravenous bolus. Symptomatic response to *Cimetidine*therapy does not preclude the presence of a gastric malignancy. There have been rare reports of transient healing of gastric ulcers despite subsequently documented malignancy.

Pregnancy: no adequate and well-controlled studies in pregnant women. Because animal reproductive studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.
Nursing Mothers: Cimetidine is secreted in human milk and, as a general rule, nursing should not be undertaken while a patient is on a drug.
Pediatric Use: Clinical experience in children is limited.
Immunocompromised Patients: In immunocompromised patients, decreased gastric acidity, including that produced by acid-suppressing agents such as cimetidine, may increase the possibility of a hyperinfection of strongyloidiasis.

Contraindications: Hypersensitivity to cimetidine, any component of the formulation, or other H2 antagonists

How supplied: Customized as per request.