

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Cimetidine Tablets 200mg

2. Qualitative and Quantitative Composition

Each tablet contains 200mg Cimetidine USP.

3. Pharmaceutical Form

Tablet.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Cimetidine is indicated in the treatment of duodenal and benign gastric ulceration, including that associated with non-steroidal anti-inflammatory agents, recurrent and stomal ulceration, oesophageal reflux disease. It is also indicated for other conditions where reduction of gastric acid by Cimetidine has been shown to be beneficial:

- persistent dyspeptic symptoms with or without ulceration, particularly meal-related upper abdominal pain, including such symptoms associated with non-steroidal anti-inflammatory agents
- the prophylaxis of gastro-intestinal haemorrhage from stress ulceration in seriously ill patients;
- before general anaesthesia in patients thought to be at risk of acid aspiration (Mendelson's) syndrome, particularly obstetric patients during labour;
- to reduce malabsorption and fluid loss in the short bowel syndrome; and
- in pancreatic insufficiency to reduce degradation of enzyme supplements.

Cimetidine is also recommended in the management of the Zollinger-Ellison syndrome.

4.2. Posology and Method of Administration

For oral administration only.

Adults

The usual adult dose is 400mg twice a day with breakfast and at bedtime. Alternatively patients with duodenal or benign gastric ulceration may be treated with a single dose of 800mg at bedtime. Regimes of 200mg thrice daily with meals and 400mg at night or, if inadequate, 400mg four times daily with meals and at bedtime may also be used. Symptomatic relief is usually rapid. Treatment should be given for 6 weeks in benign gastric ulcers, and for 8 weeks in ulcers associated with continued non-steroidal anti-inflammatory agents.

The maintenance dose for patients who would benefit from reduction of gastric secretion and in patients with benign peptic ulcer disease is 400mg at bedtime. Alternatively 400mg in the morning and at bedtime can be used.

Antacids may be used concurrently if required.

In oesophageal reflux 400mg four times daily with meals and at bedtime for 4 to 8 weeks is recommended to heal oesophagitis and relieve associated symptoms.

In patients with very high gastric acid secretion (e.g. Zollinger-Ellison syndrome) it may be necessary to increase the dose to 400mg four times daily or occasionally higher.

In the prophylaxis of haemorrhage from 'stress' ulceration doses up to a maximum of 2.4g daily may be given in divided doses. 200-400mg doses can be given every 4 to 6 hours.

In the prophylaxis of acid aspiration (Mendelson's syndrome) a single dose of 400mg may be given 90-120 minutes before induction of general anaesthesia or, in obstetric practice, at the start of labour. While such a risk persists, a dose of up to 400mg may be repeated at 4 hourly intervals as required, up to the usual maximum of 2.4g/day. The usual precautions to avoid acid aspiration should be taken.

In short bowel syndrome e.g. following substantial resection for Crohn's disease, the usual dosage range (as above) can be used according to individual response.

In pancreatic insufficiency, for protection of pancreatic enzyme supplements, 800-1600mg/day may be given according to response, in four divided doses, one to one-and-a-half hours before meals.

Dosage should be reduced in patients with impaired renal function when creatinine clearance is below 50ml/minute.

<u>Creatinine Clearance</u>	<u>Daily Dosage</u>
30 - 50 ml/minute	200mg four times daily
15 - 30 ml/minute	200mg three times daily
0 - 15 ml/minute	200mg twice daily

Cimetidine is removed by haemodialysis, but not to any significant extent by peritoneal dialysis.

Elderly

The normal adult dose may be used in the elderly unless renal function is markedly impaired.

Children

In children older than one year, Cimetidine 25mg - 30mg/kg body weight per day in divided doses may be administered.

Cimetidine tablets are unsuitable for children under one year old.

4.3. Contra-indications

There are no known contraindications to Cimetidine, other than hypersensitivity to Cimetidine.

4.4. Special Warnings and Precautions for Use

Care should be exercised in patients with renal and hepatic impairment.

Before initiation of Cimetidine therapy for any gastric ulceration, malignancy should be excluded by endoscopy, and biopsy if possible. Treatment with Cimetidine can mask symptoms and assist transient healing of gastric cancer. The consequences of a potential delay in diagnosis should be kept in mind, particularly in patients of middle age or over, or with new or recently changed dyspeptic symptoms.

Patients on prolonged Cimetidine therapy should be kept under regular surveillance with particular attention to the pathology of the gastrointestinal tract.

In patients on drug treatment or with illnesses which could cause a fall in blood cell counts, the possibility that H₂ receptor antagonism could potentiate this effect should be borne in mind.

Care should be taken that patients with a history of peptic ulcer, particularly the elderly, being treated with Cimetidine and a non-steroidal anti-inflammatory agent are observed regularly.

4.5. Interactions with other Medicaments and other forms of Interaction

Cimetidine retards the oxidative phase of hepatic drug metabolism by binding to microsomal cytochrome P450.

Clinical effects due to the potentiation of drugs such as benzodiazepines and some beta-adrenoceptor blocking agents are unlikely to be noticed, but may be important where drugs such as phenytoin, warfarin and theophylline are in use, where the margin between toxic and therapeutic concentrations is small. Close monitoring of patients on Cimetidine receiving oral anticoagulants, phenytoin, theophylline or intravenous lignocaine is recommended. A reduction in their dosage may be necessary.

4.6. Pregnancy and Lactation

Although tests in animals and clinical evidence have not revealed any hazards from the administration of Cimetidine during pregnancy or lactation, both animal and human studies have shown that it does cross the placental barrier and is excreted in milk. As with most drugs, the use of Cimetidine should be avoided during pregnancy and lactation unless essential.

4.7. Effects on Ability to Drive and Use Machines

None known

4.8. Undesirable Effects

Adverse reactions are infrequent; diarrhoea, dizziness or rash, usually mild and transient, and tiredness have been reported. Gynaecomastia has been reported and is almost always reversible on discontinuing treatment. Biochemical or biopsy evidence of reversible liver damage has been reported occasionally. Reversible confusional states have occurred, usually in elderly or already very ill patients, e.g. those with renal failure. Thrombocytopenia and leucopenia, including agranulocytosis (see Precautions), reversible on withdrawal of treatment, have been reported rarely; pancytopenia and aplastic anaemia have been reported very rarely. There have been very rare reports of interstitial nephritis, acute pancreatitis, fever, headache, myalgia, arthralgia,

sinus bradycardia, tachycardia and heart block, all reversible on withdrawal of treatment. In common with other H₂-receptor antagonists, there have been very rare reports of anaphylaxis. Alopecia has been reported but no causal relationship has been established. Reversible impotence has also been very rarely reported but no causal relationship has been established at usual therapeutic doses. Isolated increases of plasma creatinine have been of no clinical significance.

4.9. Overdose

Induction of vomiting and/or gastric lavage may be employed, together with symptomatic and supportive therapy.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Cimetidine is a histamine H₂ receptor antagonist which rapidly inhibits both basal and stimulated gastric secretion of acid and reduces pepsin output.

5.2. Pharmacokinetic Properties

Cimetidine is absorbed from the gastro-intestinal tract and peak plasma concentrations are obtained about an hour after administration on an empty stomach and about 2 hours after administration with food. The duration of action is prolonged by administration with food. Over two thirds of a dose is excreted in the urine within 24 hours.

5.3. Preclinical Safety Data

Animal studies of acute toxicity carried out, show Cimetidine to be moderately toxic by ingestion.

6. PHARMACEUTICAL PARTICULARS

6.1. List of Excipients

Microcrystalline Cellulose

BP

Maize Starch	BP
Povidone K29-32	BP
Sodium Starch Glycollate	BP
Magnesium Stearate	BP

COATING

Opadry OY-S-8826	HSE
Purified Water	BP
Carnauba Wax	BP

OPADRY OY-S-8826 INDIVIDUAL EXCIPIENTS

Hydroxypropylmethylcellulose	BP
Hydroxypropylcellulose	USNF
Titanium Dioxide	BP
Polyvinylpyrrolidone	USP
Polyethylene Glycol 400	
Iron Oxide Yellow	E172
Indigo Carmine Aluminium Lake	E132
Iron Oxide Black	E172

6.2 Incompatibilities

None known.

6.3 Shelf life

48 months.

6.4. Special Precautions for Storage

Protect from light.
Store in a dry place below 25°C.

6.5. Nature and Contents of Container

Blister/foil strips in packs of 28, 56, 60, 112 and 120 tablets.

Polypropylene pots with white polyethylene caps with optional use of polyethylene ullage filler in packs of 50, 500 or 5000 tablets.

6.6. Instruction for Use, Handling and Disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Generics [UK] Limited
Station Close
Potters Bar
Hertfordshire
EN6 1TL

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PL 04569/0206

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