Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Cimetidine Tablets 400 mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains cimetidine 400mg.

3 PHARMACEUTICAL FORM

Film-coated tablets.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

In the treatment of benign ulceration of oesophagus, stomach, upper intestinal tract (including post-operative stomal area) and the Zollinger-Ellison syndrome.

In the management of other conditions benefiting from reduced gastric acid secretion.

In the long term maintenance management of benign peptic ulcer disease under regular surveillance.

4.2 Posology and method of adminstration

For oral administration.

Adults:

The usual dose is 400 mg 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 200 mg thrice daily with meals and 400 mg nocte or, if inadequate, 400 mg q.d.s. with meals and at bedtime may also be used.

In oesophageal reflux disease 400 mg q.d.s. with meals and at bedtime for 4 to 8 weeks is recommended.

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

Treatment should be given initially for at least 4 weeks (6 weeks in the case of benign ulcer). In patients who may benefit from a reduction of gastric secretion, dosage may be reduced to a maintenance of 400 mg at bedtime, or in the morning and at bedtime.

A similar maintenance regime may be used to prevent relapse in patients with benign peptic ulceration. Patients on prolonged treatment (particularly those treated for one year) should be kept under regular surveillance.

Antacids may be used concurrently if required.

In the prophylaxis of haemorrhage from ‘stress’ ulceration doses up to a maximum of 2.4 g daily may be given in divided doses. 200-400 mg doses can be given every 4 to 6 hours by oral, nasogastric or parenteral routes (N.B. by direct intravenous injection a dose of 200mg should not be exceeded – see parenteral dosage recommendations).

In the prophylaxis of acid aspiration (Mendelson's Syndrome) a single dose of 400 mg 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 400 mg may be repeated (parenterally if appropriate) at 4 hourly intervals as required, up to the usual maximum of 2.4 g/day.

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

The total daily dose by any route should not usually exceed 2400 mg.

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

Creatinine Clearance	Daily dosage
30 - 50 ml/minute	200 mg q.d.s.
15 - 30 ml/minute	200 mg t.d.s.
0 - 15 ml/minute	200 mg b.d.

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

Elderly

The normal adult dosage may be used unless renal function is markedly impaired.

Children

Experience in children is less than that in adults. In children more than 2 years old, cimetidine 25-30 mg/kg body weight/day in divided doses may be administered by either the oral or parenteral routes.

The use of cimetidine in children less than 2 years old is not fully evaluated.

4.3 Contraindications

Hypersensitivity to cimetidine or any other ingredients of the preparation.

4.4 Special warnings and special precautions for use

1. Confusional states, mood and behavioural changes, insomnia, may occur especially in the elderly or in the very ill or those with renal failure. Those on high dosage are particularly at risk. These states are usually reversible.

2. 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.

3. The safety of prolonged use is not fully established and care should be taken to keep patients on prolonged treatment (particularly those treated to greater than one year) under regular surveillance.

4. In patients on drug treatment or with illnesses which could cause falls in blood cell counts, the possibility that H_2 receptor antagonism could potentiate this effect should be borne in mind.

4.5 Interaction with other medicinal products and other forms of interaction

Cimetidine can prolong the elimination of drugs metabolised by oxidation in the liver. Pharmacological interactions with a number of drugs e.g. diazepam, propranolol, have been demonstrated; only those with oral anticoagulants,

phenytoin and theophylline appear to date to be of clinical significance. Close monitoring of patients on cimetidine receiving oral anticoagulants, phenytoin, theophylline is recommended. A reduction in their dosage may be necessary.

4.6 Pregnancy and lactation

Cimetidine should not be administered during pregnancy or lactation in women breast-feeding infants unless considered essential by the physician. Animal studies of reproduction have shown no drug-related abnormality. Significant levels of drug reach breast milk.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

Gynaecomastia has been reported with cimetidine. Diarrhoea, dizziness, rash, tiredness have also occurred. Evidence of reversible liver damage has been reported and acute pancreatitis, interstitial nephritis with occasional increases in plasma creatinine, thrombocytopenia, headache, myalgia, arthralgia. Reversible impotence has been reported but no causal relationship established at usual therapeutic doses.

4.9 Overdose

Acute overdosage of up to 20 grams has been reported several times with no significant ill effects. 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 H_2-receptor antagonist.

5.2 Pharmacokinetic properties

Cimetidine is well absorbed after oral dosing. It is metabolised in the liver and excreted mainly through the kidney with a T½ of about 3-4 hours. The effects on acid secretion are of longer duration.

5.3 Preclinical safety data

No data is presented due to the widespread use for many years of products containing cimetidine.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Magnesium Stearate
Maize Starch
Microcrystalline Cellulose
Povidone
Talc
Hypromellose
Macrogol 400
Titanium Dioxide (E171)

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

Three Years.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

The tablets are packed in amber glass bottles with white closures of LD-polyethylene, polypropylene securitainers with tamper evident polyethylene caps and blister strips of clear PVC 250 µm thick and A1 foil hard tempered, 20 µm thick. Pack sizes are 30, 50, 60, 100 and 120 tablets.

6.6 Instructions for use and handling

None.

7 MARKETING AUTHORISATION HOLDER

Olinka (UK) Limited,
38/40 Chamberlayne Road,
London, NW10 3JE,
United Kingdom.

8 MARKETING AUTHORISATION NUMBER

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