Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Cimetidine 200 mg Stada Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Cimetidine 200mg

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Tablet.

White, round, biconvex tablet, imprinted ‘H1’.

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 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 800 mg 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.

If 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.

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.

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.

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

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 two years old, cimetidine 25-30 mg/kg body weight/day in divided doses may be administered by either the oral or parenteral routes. The maximum daily dosage should not exceed 1600 mg/day split in four divided doses.

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

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 falls in blood cell counts, the possibility that H_2 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 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 or theophylline is recommended. A reduction in their dosage may be necessary. Conversely, upon discontinuation of Cimetidine, the dose of drug simultaneously administered may require to be increased.

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, particularly on prolonged and/or high doses. 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.

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

Very rarely, heart block and anaphylaxis have been reported.

4.9 Overdose

Acute overdosage of up 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 which rapidly inhibits both basal and stimulated gastric secretion of acid and reduces pepsin output.

5.2 Pharmacokinetic properties

Cimetidine is well absorbed after oral dosing. Peak plasma levels are obtained approximately one hour after oral dosing. Food taken concomitantly delays the rate and possibly also the extent of absorption, peak plasma levels being reached after two hours.

Bioavailability is 60-70% due to first pass metabolism. Plasma protein binding is weak, and in the region of 20%.

Cimetidine is metabolised in the liver and excreted mainly through the kidney with a T½ of about 3 hours,

increased in renal impairment. The effects on acid secretion are of longer duration.

Cimetidine crosses the placental barrier and is excreted into milk.

5.3 Preclinical safety data

Acute toxicity studies in animals have not shown any particular sensitivity.

Chronic toxicity studies (oral) in rats and dogs for up to 12 months demonstrated a weak antiandrogenic effect after very high doses which was reversible on discontinuation of the drug.

No tumorigenic or mutagenic potential has been observed.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline cellulose
Maize starch
Povidone
Sodium laurilsulfate
Sodium starch glycollate
Magnesium stearate

6.2 Incompatibilities

Not applicable

6.3 Shelf Life

5 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

AL/PVC blister strips. Packs of 120 tablets.

6.6 Instructions for use and handling

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Stada Arzneimittel AG
Stadastrasse 2-18,
D-61118 Bad Vilbel
Germany

8 MARKETING AUTHORISATION NUMBER

PA 593/7/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 25th June 1999
Date of last renewal: 25th June 2004

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July 2004