Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Pinamet 400 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 400 mg of cimetidine.

For excipients, see Section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablets
Pale green, oblong, bi-convex film-coated tablet, marked ‘2Y1’ on one face.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

In the therapeutic management 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 administration

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. Regimens of 200 mg thrice daily with meals and 400 mg nocte or, if inadequate, 400 mg four times a day (q.d.s.) with meals and at bedtime may also be used. In oesophageal reflux 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.

Patients on maintenance treatment (particularly those treated for more that one year) should be kept under regular surveillance.

A similar maintenance regime may be used to prevent relapse in patients with benign peptic ulceration.

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 (NB by direct intravenous injection, a dose of 200 mg should not be exceeded - see parental 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 daily 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 oral or parenteral routes.

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

4.3 Contraindications

Hypersensitivity to cimetidine.

4.4 Special warnings and 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 a 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 gastric tract.

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

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

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 these 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 breastfeeding infants unless considered essential by the physician. Animal studies of reproduction have shown no drug-related abnormalities. Significant levels of drug reach breast milk.

4.7 Effects on ability to drive and use machines

These tablets may cause dizziness. Patients who experience dizziness should refrain from driving or operating machinery.

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 increase in plasma creatinine, thrombocytopenia, headache, myalgia, arthralgia. Reversible impotence has been reported but not casual relationship established at usual therapeutic doses.

Thrombocytopenia and leucopenia including agranulocytosis reversible on withdrawal of treatment have been reported rarely, pancytopenia and aplastic anemia have been reported very rarely.

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

4.9 Overdose

Acute overdose of up to 20 g 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 H2-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, metabolised in the liver and excreted mainly through the kidney with half-life of about 3-4 hours. The effects on acid secretion are of longer duration.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet Core:
Lactose monohydrate
Sodium starch glycollate

Povidone
Microcrystalline Cellulose
Magnesium stearate

Film-Coating:
Opadry OY5800 HSE
- Quinoline Yellow (E104)
- Indigo Carmine (E132)
- Titanium Dioxide (E171)
- Macrogol 400
- Methylcellulose
Carnauba Wax

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

3 years.

6.4 Special precautions for storage

Do not store above 25°C. Store in original container.

6.5 Nature and contents of container

Standard polypropylene and polyethylene tablet containers with HDPE lids, containing 500 tablets. Blister packs of uPVC and aluminium foil enclosed in a printed carton, containing 60 or 120 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special instructions.

7 MARKETING AUTHORISATION HOLDER

Pinewood Laboratories Limited, trading as Pinewood Healthcare
Ballymacarbry
Clonmel
Co. Tipperary

8 MARKETING AUTHORISATION NUMBER

PA 281/92/2

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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