Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Tagamet Tablets 800mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 800mg cimetidine.

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet
Pale green, oval, film-coated tablets, engraved ‘SK & F’ and ‘T800’ on one side.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Tagamet is a histamine H_2-receptor antagonist which rapidly inhibits both basal and stimulated gastric secretion of acid and reduces pepsin output.
Tagamet 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 and other conditions where reduction of gastric acid by Tagamet has been shown to be beneficial. Tagamet is also recommended in the management of the Zollinger-Ellison syndrome.

4.2 Posology and method of administration

The total daily dose should not normally exceed 2.4 g. Dosage should be reduced in patients with impaired renal function (see *Section 4.4*).

ADULTS

Oral: For patients with duodenal or benign gastric ulceration, a single daily dose of 800 mg at bedtime is recommended. Otherwise the usual dosage is 400 mg twice a day with breakfast and at bedtime. Other effective regimens are 200 mg three times a day with meals and 400 mg at bedtime (1.0 g/day) and, if inadequate, 400 mg four times a day (1.6 g/day) also with meals and at bedtime.

Treatment should be given initially for at least four weeks (six weeks in benign gastric ulcer, eight weeks in ulcer associated with continued non-steroidal anti-inflammatory agents) even if symptomatic relief has been achieved sooner. Most ulcers will have healed by that stage, but those that have not will usually do so after a further course of treatment. Treatment may be continued for longer periods in those patients who may benefit from reduction of gastric secretion and the dosage may be reduced in those whohave responded to treatment, for example to 400 mg at bedtime or 400 mg in the morning and at bedtime.
In patients with benign peptic ulcer disease who have responded to the initial course, relapse may be prevented by continued treatment, usually with 400 mg at bedtime; 400 mg in the morning and at bedtime has also been used. Patients on prolonged treatment (particularly those treated for more than one year) should be kept under regular surveillance.

In oesophageal reflux disease, 400 mg four times a day, with meals and at bedtime, for four to eight 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 400 mg four times a day, or in occasional cases further.
Since Tagamet may not give immediate symptomatic relief, antacids can be made available to all patients until symptoms disappear.
In the prophylaxis of haemorrhage from stress ulceration in seriously ill patients, doses of 200 - 400 mg can be given every four to six hours, by oral or nasogastric routes. In patients thought to be at risk of acid aspiration syndrome an oral dose of 400 mg can 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 at four-hourly intervals as required up to the usual daily maximum of 2.4 g. The usual precautions to avoid acid aspiration should be taken.
In the short bowel syndrome, e.g. following substantial resection for Crohn's disease, the usual dosage range (see above) can be used according to individual response.
To reduce degradation of pancreatic enzyme supplements, 800 - 1600 mg a day may be given according to response in four divided doses, one to one and a half hours before meals.

ELDERLY

The normal adult dosage may be used unless renal function is markedly impaired (see *Section 4.4*).

CHILDREN

Experience in children is less than that in adults. In children more than two years old, Tagamet 25 - 30 mg/kg body weight per day in divided doses may be administered. The use of Tagamet in infants under two years old is not fully evaluated; 20 mg/kg body weight per day in divided doses has been used.

4.3 Contraindications

Hypersensitivity to cimetidine.

4.4 Special warnings and precautions for use

Dosage should be reduced in patients with impaired renal function according to creatinine clearance. The following dosages are suggested: creatinine clearance of 0 to 15 ml per minute, 200 mg twice a day; 15 to 30 ml per minute, 200 mg three times a day; 30 to 50 ml per minute, 200 mg four times a day; over 50 ml per minute, normal dosage. Cimetidine is removed by haemodialysis, but not to any significant extent by peritoneal dialysis.
Clinical trials of over six years' continuous treatment and more than 15 years' widespread use have not revealed unexpected adverse reactions related to long-term therapy. The safety of prolonged use is not, however, fully established and care should be taken to observe periodically patients given prolonged treatment.
Before initiating treatment with cimetidine for any gastric ulceration, malignancy should be excluded by endoscopy and biopsy if possible.
Tagamet treatment can mask the symptoms and allow transient healing of gastric cancer. The potential delay in diagnosis should particularly be borne in mind in patients of middle age and over with new or recently changed dyspeptic symptoms.
Care should be taken that patients with a history of peptic ulcer, particularly the elderly, being treated with Tagamet and a non-steroidal anti-inflammatory agent are observed regularly.

4.5 Interaction with other medicinal products and other forms of interaction

Tagamet can prolong the elimination of drugs metabolised by oxidation in the liver. Although pharmacological interactions with a number of drugs, e.g. diazepam, propranolol, have been demonstrated, only those with oral anticoagulants, phenytoin, theophylline and intravenous lignocaine appear, to date, to be of clinical significance. Close monitoring of patients on Tagamet receiving oral anticoagulants, phenytoin or theophylline is recommended and a reduction in the dosage of these drugs may be necessary.

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

4.6 Pregnancy and lactation

Although tests in animals and clinical evidence have not revealed any hazards from the administration of Tagamet 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 Tagamet should be avoided during pregnancy and lactation unless essential.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

Over 56 million patients have been treated with Tagamet worldwide and adverse reactions have been infrequent. Diarrhoea, dizziness or rash, usually mild andtransient, 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, as have rare cases of hepatitis. Reversible confusional states sometimes associated with mood and behavioural changes or insomnia have occurred, usually in elderly or already very ill patients, (e.g. those with renal failure on high dosage).
Hallucination has been reported rarely; depression has been reported infrequently. Thrombocytopenia and leucopenia, including agranulocytosis (see *Section 4.4*), 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 H_2-receptor antagonists, there have been very rare reports of anaphylaxis. Rare cases of hypersensitivity vasculitis have been reported. These usually clear on withdrawal of the drug. 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

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 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 administration, metabolised in the liver and excreted mainly through the kidney with a half-life of about two hours. The effects on acid secretion are of longer duration.

5.3 Preclinical safety data

No additional data.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline cellulose (E460)
Povidone
Sodium lauryl sulphate
Magnesium stearate (E572)
Sodium starch glycollate
Iron oxides (E172)
Indigo carmine (E132)
Titanium dioxide (E171)
Hydroxypropylmethylcellulose (E464)
Propylene glycol
Disodium edetate
Talc (E553(b))
Carnauba wax (E903)
The sodium content of the tablets is 1.6 mg.

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

The shelf life expiry date of this product is the date shown on the container and outer carton of the product as marketed in the country of origin.

6.4 Special precautions for storage

No special precautions for storage.

6.5 Nature and contents of container

Opaque calendar packs (OP) of 30 tablets (2 x 15), packed in a cardboard carton.

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 requirements.

7 Parallel Product Authorisation Holder

PRIMECROWN LTD.,
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Uxbridge,
Middlesex UB8 2RZ,
ENGLAND

8 Parallel Product Authorisation Number

PPA 1071/012/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 08 August 2003