Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Zantac Tablets 150 mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains ranitidine 150 mg (as the hydrochloride).

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet.

White, film-coated, round tablets engraved ‘GX EC2’ on one face and plain on the other.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Duodenal ulcer and benign gastric ulcer, including that associated with non-steroidal anti-inflammatory agents.

Prevention of non-steroidal anti-inflammatory drug associated duodenal ulcers especially in patients with a history of peptic ulcer disease.

Post-operative ulcer.

Oesophageal reflux disease including long term management of healed oesophagitis. Symptomatic relief in gastro-oesophageal reflux disease.

Zollinger-Ellison Syndrome.

Prophylaxis of recurrent haemorrhage with bleeding peptic ulcers.

Before general anaesthesia in patients at risk of acid aspiration (Mendelson's syndrome), particularly obstetric patients during labour.

Treatment of other conditions where reduction of gastric acid secretion is likely to be beneficial.

4.2 Posology and method of administration

Adults:
Duodenal ulcer, gastric ulcer:
The standard dosage regimen is 150 mg twice daily or 300 mg at night. It is not necessary to time the dose in relation to meals. This may be increased to 300mg twice daily without an increased incidence of side effects.Subsequently, a maintenance dose of 150mg at night may be used. Smoking is associated with a higher rate of ulcer relapse, and such patients should be advised to stop smoking. In those who fail to comply with such advice, a dose of 300mg at night provides additional therapeutic benefit over the standard dose.

In most cases of duodenal ulcer, benign gastric ulcer and post-operative ulcer, healing occurs within 4 weeks. Healing

usually occurs after a further 4 weeks of treatment in those not fully healed after the initial course of therapy. In ulcers following NSAID therapy or associated with continued NSAID's, 8-12 weeks treatment may be necessary with 150mg twice daily or 300mg at night. For the prevention of NSAID associated duodenal ulcers 150 mg twice daily may be given concomitantly with NSAID therapy.

Gastro-oesophageal reflux disease:
Symptom relief in gastro-oesophageal reflux disease. In patients with gastro-oesophageal reflux disease, a dose regimen of 150 mg twice daily for 2 weeks is recommended and this can be repeated in patients in whom the initial symptomatic response is inadequate

Oesophageal reflux disease:
In the management of oesophageal reflux disease, the recommended course of treatment is either 150 mg twice daily or 300 mg at bedtime for up to 8 weeks or 12 weeks if necessary.

In patients with moderate to severe oesophagitis, the dosage of ranitidine may be increased to 150 mg 4 times daily for up to 12 weeks. The increased dose has not been associated with an increased incidence of unwanted effects.

Healed oesophagitis:
For long term treatment, recommended adult dose is 150 mg twice daily. Long term treatment is not indicated in management of patients with unhealed oesophagitis with or without Barrett's epithelium.

In keeping with the recommended clinical practice, it is advisable that patients on long-term maintenance therapy receive regular routine assessment by their practitioners.

Zollinger-Ellison syndrome:
The starting dose for Zollinger-Ellison syndrome is 150 mg three times daily, and this may be increased as necessary. Doses up to 6 grams per day have been well tolerated.

Prophylaxis of acid aspiration (Mendelson's) syndrome:

150 mg oral dose can be given 2 hours before anaesthesia, and preferably also 150 mg the previous evening. In obstetric patients in labour 150 mg every 6 hours, but if general anaesthesia is required it is recommended that a non-particulate antacid (e.g. sodium citrate) be given in addition.

The usual precautions to avoid acid aspiration should also be taken.

Children:
The recommended oral dose for the treatment of peptic ulcer in children is 2 mg/kg to 4 mg/kg twice daily to a maximum of 300 mg ranitidine per day.

Renal Impairment:
Accumulation of ranitidine with resulting elevated plasma concentrations will occur in patients with severe renal impairment. Accordingly, it is recommended that the daily dose of ranitidine in such patients should be 150 mg at night for 4-8 weeks. The same dose should be used for maintenance treatment, if necessary. In patients on dialysis, dosage should be given on completion of dialysis.

4.3 Contraindications

Ranitidine is contra-indicated in patients known to have hypersensitivity to any component of the preparation.

4.4 Special warnings and precautions for use

In keeping with the recommended clinical practice, it is advisable that patients on long-term maintenance therapy receive regular routine assessment by their practitioners.

Malignancy:
The possibility of malignancy should be excluded before commencement of therapy in patients with gastric ulcer (and if indications include dyspepsia, patients of middle age and over with new or recently changed dyspeptic symptoms) as treatment with ranitidine may mask symptoms of gastric carcinoma.

Renal Disease:
Ranitidine is excreted via the kidney and so plasma levels of the drug are increased in patients with severe renal impairment.

The dosage should be adjusted as detailed above under Dosage in Renal Impairment.

Regular supervision of patients who are taking non-steroidal anti-inflammatory drugs concomitantly with ranitidine is recommended, especially in the elderly and in those with a history of peptic ulcer.

Rare clinical reports suggest that ranitidine may precipitate acute porphyric attacks. Ranitidine should therefore be avoided in patients with a history of acute porphyria

4.5 Interaction with other medicinal products and other forms of interaction

Ranitidine does not inhibit the hepatic cytochrome P450-linked mixed function oxygenase system. Accordingly, ranitidine does not potentiate the actions of drugs which are inactivated by this enzyme; these include diazepam, lignocaine, phenytoin, propranolol, theophylline and warfarin.

4.6 Pregnancy and lactation

Ranitidine crosses the placenta and is excreted in human breast milk.

Ranitidine should only be used during pregnancy or lactation if considered essential by the physician.

4.7 Effects on ability to drive and use machines

There are no known effects on the ability to drive and use machines.

4.8 Undesirable effects

The following have been reported as events in clinical trials or in the routine management of patients treated with ranitidine. The relationship to ranitidine therapy has not been established in many cases.

Transient and reversible changes in liver function tests can occur. There have been occasional reports of hepatitis (hepatocellular, cholestatic or mixed) with or without jaundice. These were usually reversible.

Acute pancreatitis has been rarely reported.

Leucopenia and thrombocytopenia have occurred rarely in patients. These are usually reversible.

Rare cases of agranulocytosis or pancytopenia, sometimes with marrow hypoplasia or aplasia have been reported.

Hypersensitivity reactions (urticaria, angioneurotic oedema, fever, bronchospasm, hypotension, anaphylactic shock) have been seen rarely following the parenteral and oral administration of ranitidine. These reactions have occasionally occurred after a single dose.

As with other H_2 receptor antagonists there have been rare reports of bradycardia and A-V block.

Headache, sometimes severe, and dizziness have been reported in a very small proportion of patients. Rare cases of reversible mental confusion, depression and hallucinations have been reported, predominantly in severely ill and

elderly patients. In addition, reversible involuntary movement disorders have been reported rarely.

There have been rare reports of reversible blurred vision suggestive of a change in accommodation.

Skin rash has been reported, including rare cases of erythema multiforme. Musculoskeletal symptoms such as arthralgia and myalgia have been reported rarely. Rare cases of vasculitis and alopecia.

Very rare cases of acute interstitial nephritis have been reported.

Reversible impotence has been reported rarely.

No clinically significant interference with endocrine or gonadal function has been reported. There have been a few reports of breast symptoms (swelling and/or discomfort) in men taking ranitidine; some cases have resolved on continued ranitidine treatment. Discontinuation of therapy may be necessary in order to establish the underlying cause.

Antibiotic associated diarrhoea may occur when amoxycillin and metronidazole are taken with ranitidine.

4.9 Overdose

Ranitidine is very specific in action and accordingly no particular problems are expected following overdosage. Symptomatic and supportive therapy should be given as appropriate. If need be, the drug may be removed from the plasma by haemodialysis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: A02 BA02

Ranitidine is a specific rapidly acting histamine H_2-antagonist. It inhibits basal and stimulated secretion of gastric acid, reducing both the volume and the acid and pepsin content of the secretion. Ranitidine has a relatively long duration of action and so a single 150 mg dose effectively suppresses gastric acid secretion for twelve hours.

5.2 Pharmacokinetic properties

Absorption of ranitidine after oral administration is rapid and peak plasma concentrations are usually achieved within two hours of administration. Absorption is not significantly impaired by food or antacids. The elimination half-life of ranitidine is approximately 2 hours. Ranitidine is excreted via the kidneys mainly as the free drug and in minor amounts as metabolites Its major metabolite is an N-oxide and there are smaller quantities of S-oxide and desmethyl ranitidine. The 24 hour urinary recovery of free ranitidine and its metabolites is about 40% with orally administered drug.

5.3 Preclinical safety data

No additional data of relevance.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline cellulose
Magnesium stearate
Hypromellose
Titanium Dioxide E171

Triacetin

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

The shelf life expiry date for this product shall be the date shown on the container and outer package of the product on the market in the country of origin.

6.4 Special precautions for storage

Do not store above 30°C.

6.5 Nature and contents of container

Aluminium foil strips or double foil blister packs in cartons of 60 tablets.

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 PARALLEL PRODUCT AUTHORISATION HOLDER

PRIMECROWN Limited
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England

8 PARALLEL PRODUCT AUTHORISATION NUMBER

PPA 1071/009/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 08 August 2003