Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Ranitidine Tablets BP 300mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 300mg of Ranitidine as Ranitidine Hydrochloride.

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Film coated tablet
Oblong biconvex white to yellowish, film coated tablet scored on one side.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Ranitidine Tablets BP are indicated for the treatment of duodenal ulcer and benign gastric ulcer.

Ranitidine Tables BP are also indicated for the treatment of post-operative ulcer, Zollinger-Ellison syndrome and oesophageal reflux disease and other conditions where reduction of gastric acid secretion is likely to be beneficial.

4.2 Posology and method of administration

Adults: The usual dosage is 150mg twice daily, taken in the morning and evening. Alternatively, patients with duodenal ulceration, gastric ulceration or oesophageal reflux disease may be treated with a single bedtime dose of 300mg. It is not necessary to time the dose in relation to meals. In most cases of duodenal ulcer, benign gastric ulcer and post-operative ulcer, healing occurs in four weeks. Healing usually occurs after a further four weeks of treatment in those patients whose ulcers have not fully healed after the initial course of therapy.

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

In patients with moderate to severe oesophagitis, the dosage of ranitidine may be increased to 150mg four times daily . In patients with Zollinger-Ellison syndrome, the starting dose is 150mg three times daily and this may be increased as necessary. Patients with this syndrome have been given increasing doses up to 6g per day and these doses have been well tolerated.

In obstetric patients at commencement of labour, an oral dose of 150mg may be given followed by 150mg at six-hourly intervals. It is recommended that since gastric emptying and drug absorption are delayed during labour, any patient requiring emergency general anaesthesia should be given, in addition, a non-particulate antacid (e.g. sodium citrate) prior to induction of anaesthesia. The usual precautions to avoid acid aspiration should also be taken.

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

Renal Insufficiency: In patients with a creatinine clearance < 50ml/min the usual dose is 150mg nightly. In patients on dialysis, dosage should be given on completion of dialysis.

Route of administration: Oral.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

Treatment with a histamine H_2-antagonist may mask symptoms associated with carcinoma of the stomach and may therefore delay diagnosis of the condition. Accordingly, where gastric ulcer has been diagnosed or in patients of middle age and over with new or recently changed dyspeptic symptoms the possibility of malignancy should be excluded before therapy with Ranitidine Tablets BP is instituted.

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

Although clinical reports of acute intermittent porphyria associated with ranitidine administration have been rare and inconclusive, ranitidine should be avoided in patients with a history of this condition.

4.5 Interaction with other medicinal products and other forms of interaction

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

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 amoxycillin, diazepam, lignocaine, phenytoin, metronidazole, propranolol, theophylline and warfarin.

4.6 Pregnancy and lactation

Ranitidine crosses the placenta but therapeutic doses administered to obstetric patients in labour or undergoing caesarean section have been without any adverse effect on labour, delivery or subsequent neonatal progress. Ranitidine is also excreted in human breast milk.

Like other drugs, Ranitidine Tablets BP should only be used during pregnancy and nursing if considered essential.

4.7 Effects on ability to drive and use machines

There have been no reported effects on the patient’s ability to drive or operate machinery whilst taking Ranitidine Tablets BP.

4.8 Undesirable effects

The following undesirable effects have been reported in 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, hepatocanalicular or mixed) with or without jaundice. These were usually reversible. Acute pancreatitis has been reported rarely.

Leucopenia and thrombocytopenia have occurred rarely in patients. These are usually reversible. Rare cases of agranulocytosis or of 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 or 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.

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

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

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 Tablets BP have a relatively long duration of action and so a single 150mg dose effectively suppresses gastric acid secretion for twelve hours.

5.2 Pharmacokinetic properties

The bioavailability of ranitidine is consistently about 50%. Absorption of ranitidine after oral administration is rapid and peak plasma concentrations are usually achieved 2-3 hours after administration. Absorption is not significantly impaired by food or antacids. Ranitidine is not extensively metabolised. Elimination of the drug is primarily by tubular secretion. The elimination half-life of ranitidine is 2-3 hours. In balance studies with 150mg 3H-ranitidine 60-70% of an oral dose was excreted in urine and 26% in faeces. Analysis of urine excreted in the first 24 hours after dosing showed that 35% of the oral dose was eliminated unchanged. About 6% of the dose is excreted as the N-oxide, 2% as the S-oxide, 2% as desmethyl ranitidine and 1-2% as the furoic acid analogue.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Croscarmellose sodium
Magnesium stearate
Microcrystalline cellulose
Film coating
Hypromellose

Titanium dioxide
Talc
Macrogol 6000
Polymethylmethacrylic acid copolymer (Eudragit E)

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

2 years.

6.4 Special precautions for storage

Do not store above 25^{o}C.

6.5 Nature and contents of container

Blister strips constructed of 20µm aluminium backed with a 40µm aluminium/25µm OPA/60µm PVC laminate, packed into a cardboard carton with a patient information leaflet. Pack sizes of 28, 30, 56 or 60 will be available for marketing.

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

For oral use only.

7 MARKETING AUTHORISATION HOLDER

Norton Healthcare Limited
Albert Basin
Royal Docks
London E16 2QJ
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA 282/71/2

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 03 April 1998

Date of last renewal: 03 April 2003

10 DATE OF REVISION OF THE TEXT

April 2003