Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Ranitidine 150mg Film-Coated Tablets.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Ranitidine Hydrochloride equivalent to ranitidine 150 mg.

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Film-coated Tablet.

Circular, biconvex, white to yellowish film-coated tablets with ‘S91’ on one side.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

The treatment of duodenal ulcer, benign gastric ulcer, reflux oesophagitis, post-operative ulcer, Zollinger-Ellison syndrome, and other conditions where reduction of gastric acid is likely to be beneficial.

4.2 Posology and method of adminstration

Route of administration: Oral.

Adults and the elderly
The usual initial dosage is 150mg twice daily or 300mg at night. This may be increased to 300mg twice daily.

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

Management of reflux oesophagitis:
The usual course of treatment is either 150mg twice daily or 300mg at night for up to eight weeks. In patients with moderate to severe oesophagitis the dosage may be increased to 150mg four times daily, alternatively 300mg twice daily, if necessary.

Zollinger-Ellison Syndrome:
The starting dose is 150mg three times daily, increased as necessary up to a maximum of 6 grams daily.

Anaesthesia:
In patients thought to be at risk of acid aspiration syndrome an oral dose of 150mg can be given 2 hours before induction of general anaesthesia, and preferably also 150mg the previous evening.

Obstetric patients
In obstetric patients an oral dose of 150mg may be given at commencement of labour, followed by 150mg at 6 hourly intervals. A non-particulate antacid e.g. sodium citrate) is also recommended prior to induction of anaesthesia in any

patient requiring emergency general anaesthesia.

Patients with severe renal impairment:
In patients with a creatinine clearance of less than 50ml/min the maximum daily dose is 150mg nightly. In patients who are anephric, but are undergoing haemodialysis, ranitidine is removed in the dialysate and dosage should be given on completion of dialysis.

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

4.3 Contraindications

Known hypersensitivity to ranitidine or any other component of the preparation.

4.4 Special warnings and special precautions for use

Treatment with a histamine H_2 -antagonist may mask symptoms associated with carcinoma of the stomach and therefore may delay diagnosis of the condition. Before initiation of ranitidine treatment for any gastric ulceration, malignancy should be excluded, by endoscopy and biopsy, if possible.

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

Patients receiving prolonged treatment should be examined periodically.

Regular supervision of patients who are taking NSAIDs concomitantly is recommended, especially in the elderly and in those with a history of peptic ulcer.

Use in renal transplants:
Ranitidine has been used in patients with renal transplants.

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 at blood levels produced by standard doses, does not inhibit the hepatic cytochrome P450-linked mixed function oxygenase system. Accordingly, ranitidine in usual therapeutic doses 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 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 should only be used during pregnancy and breast-feeding if considered essential by the physician.

4.7 Effects on ability to drive and use machines

Patients should be warned not to drive or operate machinery if they experience dizziness when taking ranitidine.

4.8 Undesirable effects

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.

Very rare cases of acute interstitial nephritis have been reported.

Blood count changes (leucopenia and thrombocytopenia) have occurred in a few 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, bronchospasm, hypotension, fever and 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, rare reports of bradycardia and A-V block have been reported.

Headache, sometimes severe, dizziness and blurred vision 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. Reversible involuntary movement disorders have been reported rarely.

Rare cases of vasculitis, alopecia and reversible impotence have been reported.

Skin rash has been reported, including rare cases suggestive of mild erythema multiforme. There have been rare reports of musculoskeletal symptoms such as arthralgia and myalgia.

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 with the drug. 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: A02B A, H_2-receptor antagonists.

Ranitidine is a specific, rapidly acting histamine H_2-receptor antagonist. It inhibits basal and stimulated secretion of gastric acid, reducing both the volume and the acid and pepsin concentration of the secretion. Ranitidine has a relatively long duration of action and so a single 150mg 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-three hours of administration.

Absorption is not significantly affected by food or antacids. The elimination half life of ranitidine is approximately two hours. Ranitidine is excreted via the kidneys mainly as the free drug and in minor amounts as metabolites. Analysis of urine excreted in the first 24 hours after dosing showed that 70% of the intravenous dose and 35% of the oral dose were eliminated unchanged. The metabolism of ranitidine is similar after both oral and intravenous dosing; about 6% of the dose excreted in urine as the N-oxide, 2% as the S-oxide, 2% as desmethylranitidine and 2% as the furoic acid analogue.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Croscarmellose sodium
Magnesium stearate
Microcrystalline cellulose
Hypromellose
Titanium dioxide
Talc
Macrogol
Polymethacrylate

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

2 years.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

Aluminium/Aluminium foil blister strips 60 tablets in a carton.

6.6 Instructions for use and handling

No special requirements.

7 MARKETING AUTHORISATION HOLDER

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