Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Zantac 75mg film-coated tablets.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 75mg rantidine as ranitidine hydrochloride.

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet.

Peach coloured five sided film-coated tablet with a “Z” engraved on one side and “75” on the other.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

The short-term symptomatic relief of acid indigestion and heartburn.

4.2 Posology and method of administration

Adults:
One Zantac 75 tablet should be taken when symptoms occur, day or night. Maximum intake in 24 hours: 2 tablets (150mg). The maximum treatment period is two weeks.

It is not necessary to take the tablets with food.

Patients are advised to consult their doctor if symptoms persist, get worse or continue for 14 days.

Children:
The use of Zantac 75 tablets in children under 16 years of age is not recommended.

4.3 Contraindications

Known 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.

Ranitidine is excreted through the kidney and so plasma levels of the drug are increased in patients with severe renal impairment. Zantac 75 are not suitable for these patients.

Rare clinical reports suggest that ranitidine may precipitate acute porphyric attacks. Ranitidine should therefore not be given to patients with a history of acute porphyria.

The following patients are advised to seek their doctor's advice before taking Zantac 75:

- Patients with severe renal and/or hepatic impairment.
- Patients under regular medical control.
- Patients taking medication prescribed by a physician or self-prescribed.
- Patients of middle age or older with new or recently changed dyspeptic symptoms.
- Patients with unintended weight loss in association with dyspeptic symptoms.
- Patients with a risk of developing ulcers or a history of peptic ulcer (e.g. patients taking NSAIDs).

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 at therapeutic doses. Accordingly, ranitidine in standard therapeutic doses does not potentiate the action of drugs which are inactivated by this enzyme; these include diazepam, lignocaine, phenytoin, propranolol, theophylline and warfarin. If high doses (2g) of sucralfate are co-administered with ranitidine the absorption of the latter may be reduced. This effect is not seen if sucralfate is taken after an interval of 2 hours.

4.6 Pregnancy and lactation

Insufficient data is available to assess the possible risks of the use of ranitidine in pregnant or lactating women. Ranitidine crosses the placenta and is also excreted in breast milk; however, the clinical relevance is not clear. Zantac 75 should therefore not be taken during pregnancy and lactation without consulting a doctor.

4.7 Effects on ability to drive and use machines

Insufficient data on the effects on ability to drive and to operate machines is available.

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 usually reversible, hepatitis (hepatocellular, cholestatic or mixed) with or without jaundice. Rarely, acute pancreatitis has been reported.

Reversible, thrombocytopenia and leucopenia have occurred in few patients. Rare cases of pancytopenia, sometimes with bone marrow hypoplasia or aplasia, and agranulocytosis have rarely been reported.

Hypersensitivity reactions (e.g. urticaria, fever and anaphylactic shock) have been seen rarely; these reactions sometimes occurred after a single parenteral or oral dose.

Headache, sometimes severe, and dizziness have been reported in a very small proportion of patients. Rare cases of reversible mental confusion, depressions and hallucinations has been reported, predominantly in severely ill and/or elderly patients. In addition reversible involuntary movement disorders have been reported rarely.

Rare cases of bradycardia and several arrhythmias like AV-block, and hypotension have been reported. There have been rare reports of reversible blurred vision suggestive of a change in accommodation. There have been a few reports of gynaecomastia in men taking ranitidine without clinically significant interference with endocrine or gonadal function.

Very rare cases of diarrhoea have been reported.

Very rare cases of acute interstitial nephritis have been reported.

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

4.9 Overdose

Ranitidine is very specific in action and accordingly no particular problems are expected following overdosage with the drug. Up to 6g per day has been administered without untoward effect in patients with Zollinger-Ellison syndrome.

In case of overdosage symptomatic and supportive therapy is recommended. If necessary, 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-receptor 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 long duration of action and a single 75mg dose effectively suppresses gastric acid secretion for at least 12 hours. Clinical studies have shown that Zantac 75 can relieve the symptoms during a maximum of twelve hours.

5.2 Pharmacokinetic properties

The bioavailability of ranitidine is consistently about 50%. Peak concentrations in plasma, normally in the range 236-270 ng/ml, after a 75 mg dose, occur 2-3 hours after oral administration. Concentrations of ranitidine in plasma are proportional to doses up to and including 300 mg.

Ranitidine is not extensively metabolised. Elimination of the drug is primarily by tubular excretion. The elimination half-life is 2-3 hours.

In balance studies with 150 mg ^{3}H-ranitidine 93% of an intravenous dose was excreted in urine and 5% in faeces; 60-70% of an oral dose was excreted in the urine and 26% in the faeces. 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 being excreted in urine as the N-oxide, 2% as the S-oxide, 2% as desmethylranitidine and 1-2% as the furoic acid analogue.

5.3 Preclinical safety data

None given.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline cellulose
Magnesium stearate
Hypromellose
Titanium dioxide E171
Glyceryl triacetate
Synthetic red iron oxide E172

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 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

Blister packs of 12 tablets contained in an outer 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

PCO Manufacturing Limited,
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8 Parallel Product Authorisation Number

PPA 0465/033/003

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 20 May 2005

10 DATE OF REVISION OF THE TEXT

October 2008