Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Zantac 75mg Film-coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Zantac 75 contains 75mg ranitidine as ranitidine hydrochloride.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet (Tablet).
Five sided biconvex, pink film coated tablet with 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

Dosage in Adults (including the elderly) and children 16 years of age or older:

One Zantac 75 tablet should be taken when symptoms appear, 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 or pharmacist if symptoms persist, get worse or continue for 14 days.

Children:

Not recommended for children under 16 years of age.

4.3 Contraindications

Known hypersensitivity to any component of the preparation.

4.4 Special warnings and precautions for use

Treatment with a histamine H2-antagonist may mask symptoms associated with carcinoma of the stomach and may therefore delay diagnosis of the condition.

Ranitidine is excreted via the kidney and so plasma levels of the drug are increased in patients with renal impairment (creatine clearance less than 50ml/min). Ranitidine products are not suitable for these patients without medical supervision.

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

The following patients are advised to seek their doctor's advice before taking ranitidine products:

Patients with renal impairment (creatine clearance less than 50ml/min) and/or hepatic impairment.
Patients under regular medical supervision.
Patients taking medications either physician prescribed 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 taking non-steroidal anti-inflammatory drugs, especially in those with a history of ulcer should consult their doctor prior to use.

In patients such as the elderly, persons with chronic lung disease, diabetes or the immunocompromised, there may be an increased risk of developing community acquired pneumonia. A large epidemiological study showed an increased risk of developing community acquired pneumonia in current users of ranitidine alone versus those who had stopped treatment, with an observed adjusted relative risk increase of 1,82 (95% CI, 1,26 - 2,64).

4.5 Interaction with other medicinal products and other forms of interaction

Ranitidine has the potential to affect the absorption, metabolism or renal excretion of other drugs. The altered pharmacokinetics may necessitate dosage adjustment of the affected drug or discontinuation of treatment.
Interactions occur by several mechanisms including:
1) Inhibition of cytochrome P450-linked mixed function oxygenase system:
Ranitidine at usual therapeutic doses does not potentiate the actions of drugs which are inactivated by this enzyme system such as diazepam, lidocaine, phenytoin, propranolol and theophylline. There have been reports of altered prothrombin time with coumarin anticoagulants (e.g. warfarin). Due to the narrow therapeutic index, close monitoring of increased or decreased prothrombin time is recommended during concurrent treatment with ranitidine.
2) Alteration of gastric pH:
The bioavailability of certain drugs may be affected. This can result in either an increase in absorption (e.g. triazolam, midazolam, glipizide) or a decrease in absorption (e.g. ketoconazole, atazanavir, delaviridine, gefitnib).

4.6 Fertility, pregnancy and lactation

Fertility

There are no data on the effects of ranitidine on human fertility. In animal studies, no effect on fertility was observed.

Pregnancy

Ranitidine crosses the placenta. As with other drugs, ranitidine products should not be taken in pregnancy without consulting a doctor.

Lactation

Ranitidine is excreted in human breast milk. Women who are breastfeeding are advised to speak to their doctor before taking ranitidine products.

4.7 Effects on ability to drive and use machines

None reported.

4.8 Undesirable effects

The following convention has been utilised for the classification of undesirable effects:
Very common (2:1/10), common (2:1/100, <1/10), uncommon (2:1/1000, <1/100), rare (2:1/10,000, <1/1000), very rare (<1/10,000). Adverse event frequencies have been estimated from spontaneous reports from post-marketing data.

Blood & Lymphatic System Disorders
Very rare: Blood count changes (leucopenia, thrombocytopenia). These are usually reversible. Agranulocytosis or pancytopenia, sometimes with marrow hypoplasia or marrow aplasia.

Immune System Disorders
Rare: Hypersensitivity reactions (urticaria, angioneurotic oedema, fever, bronchospasm, hypotension and chest pain).
Very rare: Anaphylactic shock.
These events have been reported after a single dose.

Psychiatric Disorders
Very rare: Reversible mental confusion, depression and hallucinations.
These have been reported predominantly in severely ill and elderly patients.

Nervous System Disorders
Very rare: Headache (sometimes severe), dizziness and reversible involuntary movement disorders.

Eye disorders
Very rare: Reversible blurred vision.
There have been reports of blurred vision, which is suggestive of a change in accommodation.

Cardiac Disorders
Very rare: As with other H2 receptor antagonists bradycardia and A-V Block.

Vascular Disorders
Very Rare: Vasculitis

Gastrointestinal Disorders
Very Rare: Acute pancreatitis. Diarrhoea.
Uncommon: Abdominal pain, constipation, nausea (these symptoms mostly improved during continued treatment).

Hepatobiliary Disorders
Rare: Transient and reversible changes in liver function tests.
Very Rare: Hepatitis (hepatocellular, hepatocanalicular or mixed) with or without jaundice, these were usually reversible.

Skin and Subcutaneous Tissue Disorders
Rare: Skin Rash
Very Rare: Erythema multiforme, alopecia.

Musculoskeletal and Connective Tissue Disorders
Very Rare: Musculoskeletal symptoms such as arthralgia and myalgia.

Renal and Urinary Disorders
Very Rare: Acute interstitial nephritis
Rare: Elevation of plasma creatinine (usually slight; normalised during continued treatment)

Reproductive System and Breast Disorders
Very Rare: Reversible impotence and breast conditions (such as gynaecomastia and galactorrhoea)

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the ADR Reporting Website: www.medicinesauthority.gov.mt/adrportal

4.9 Overdose

Symptoms and Signs

Ranitidine is very specific in action and no particular problems are expected following overdosage with ranitidine formulations.

Treatment

Symptomatic and supportive therapy should be given as appropiate.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code: A02BA02

Pharmacotherapeutic group: 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 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 3H-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.

Special patient populations: In patients over 50 years of age, half-life is prolonged (3-4 h) and clearance is reduced, consistent with the age-related decline of renal function. However, systematic exposure and accumulation are 50% higher. This difference exceeds the effect of declining renal function, and indicates increased bioavailability in older patients.

5.3 Preclinical safety data

Non-clinical data revealed no special hazard for humans based on conventional studies of safety pharmacology, repeated-dose toxicity, genotoxicity, carcinogenic potential and toxicity to reproduction and development.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet Core
Microcrystalline cellulose
Magnesium stearate

Tablet Coat
Hypromellose
Titanium dioxide E171
Triacetin
Synthetic red iron oxide E172

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store below 25°C.
Tablets should not be removed from blisters until immediately prior to use.

6.5 Nature and contents of container

Double aluminum/polyethylene foil blisters packed in cartons containing 2, 6, 12 or 24 tablets.
Not all pack sizes may be marketed.

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 MARKETING AUTHORISATION HOLDER

Chefaro Ireland DAC,
Treasury Building
Lower Grand Canal Street
Dublin 2
Ireland

8 MARKETING AUTHORISATION NUMBER

MA 1005/00201

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 18th September 2006

Date of last renewal: 26th September 2011

10 DATE OF REVISION OF THE TEXT

2nd April 2018