Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Ranitic 75 mg Film-coated tablets.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains ranitidine 75 mg (as ranitidine hydrochloride) equivalent to 75 mg ranitidine.
Excipients with known effect: also includes 1.55 mg lactose (as monohydrate) and a maximum of 0.135 mg sodium per tablet.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet

Yellow, round and biconvex tablets with one- sided score notch. The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the short term symptomatic relief of acid indigestion and heartburn.

4.2 Posology and method of administration

Route of Administration: Oral.

Adults and children over 16:

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

It is not necessary to take the tablets with food.

If symptoms persist, get worse or continue for more than 2 weeks please consult your doctor.

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

4.3 Contraindications

Hypersensitive to the active substance or to the ingredients of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

The possibility of malignancy should be excluded before commencement of therapy in patients with gastric ulcer as treatment with ranitidine may mask symptoms of gastric carcinoma.
Ranitidine is excreted via the kidney and so plasma levels of the active substance are increased in patients with renal impairment (creatine clearance less than 50ml/min). Ranitic 75 mg is not suitable for these patients without 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. 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 H2 receptor antagonist versus those who had stopped treatment, with an observed adjusted relative risk increase of 1,82 (95% CI, 1,26 - 2,64).

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

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

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption, should not take this medicine.

This medicine contains less than 1 mmol (23 mg) sodium per tablets, that is to say essentially 'sodium-free'.

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 dose does not potentiate the actions of medicinal products which are inactivated by this enzyme; 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 medicinal products 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, gefitinib).

If high doses (2 g) of sucralfate are co-administered with ranitidine the absorption of the latter may be reduced. The effect is not seen if sucralfate is taken after an interval of 2 hours. There is no evidence of an interaction between ranitidine and amoxycillin or metronidazole.

4.6 Fertility, Pregnancy and lactation

Fertility
There are no data on the effects of ranitidine on human fertility. There were no effects on male and female fertility in animal studies.

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

Not applicable

4.8 Undesirable effects

The following convention has been utilised for the classification of undesirable effects: Very common (≥1/10), common (≥1/100, <1/10), uncommon (≥1/1000, <1/100), rare (≥1/10,000, <1/1000), very rare (<1/10,000). Not known (cannot be estimated from the available data).

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, A-V Block and tachycardia.

Vascular Disorders
Very Rare: Vasculitis.

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

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
Rare: Elevation of plasma creatinine (usually slight; normalised during continued treatment)
Very Rare: Acute interstitial nephritis.

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

Paediatric population
The safety of ranitidine has been assessed in children aged 0 to 16 years with acid-related disease and was generally well tolerated with an adverse event profile resembling that in adults. There are limited long term safety data available in particular regarding growth and development.

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 professions are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie ; E-mail: medsafety@hpra.ie .

4.9 Overdose

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

Treatment:
Symptomatic and supportive therapy should be given as appropriate.

5 PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Alimentary tract and metabolism.
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 75 mg dose effectively suppresses gastric acid secretion for twelve hours. Clinical studies have shown that Ranitidine 75 mg 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.

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

Microcrystalline cellulose
Calcium hydrogen phosphate dihydrate
Maize starch

Sodium starch glycolate (Type A)
Magnesium stearate
Colloidal anhydrous silica
Lactose monohydrate
Hypromellose
Titanium dioxide (E 171)
Macrogol 4000
Yellow ferric oxide

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

3 years.

6.4 Special precautions for storage

Do not store above 25°C. Store in the original package.

6.5 Nature and contents of container

Cartons of 7, 14 and 28 tablets, in aluminium foil strips or push through double foil blister packs.

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

Rowex Ltd.
Bantry
Co Cork.

8 MARKETING AUTHORISATION NUMBER

PA0711/024/004

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 16 May 2003
Date of last renewal: 16 June 2007

10 DATE OF REVISION OF THE TEXT

31 January 2019