# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

Ranitidine 75mg Film-coated Tablets

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Ranitidine 75mg Film-coated Tablets.

Each tablet contains 83.7mg ranitidine hydrochloride equivalent to 75 mg ranitidine

For the full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Film-coated Tablets

Cream yellow round, biconvex, film-coated tablets having approximately 7 mm diameter with the inscription "IT" on one side and plain on the other side.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic Indications

Symptomatic treatment of heartburn and acid reflux.

### 4.2 Posology and method of administration

**Adults:**

One tablet when symptoms occur, during the day or at night. Most patients find 1 or 2 tablets in a 24-hour period satisfactory. A maximum of 4 tablets may be taken in a period of 24 hours.

It is not necessary to take the tablets with meals.

The maximum treatment duration with ranitidine is 14 days. If the symptoms persist after 14 days, fail to improve or even worsen, consultation with a doctor or pharmacist is advised.

**Renal impairment:**

In patients with significant renal insufficiency (creatinine clearance <50 ml/min), accumulation of ranitidine can occur, resulting in an increased plasma concentration. It is recommended that patients, in consultation with their physician (see 4.4), should take no more than 2 tablets every 24 hours.

**Children:**

Use of ranitidine tablets in children younger than 16 years is not recommended.

### 4.3 Contraindications

Known hypersensitivity to ranitidine or to any of the other ingredients of Ranitidine 75 tablets.

### 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.

Patients of middle age or older experiencing dyspeptic symptoms for the first time or experiencing a significant change in dyspeptic symptoms, or patients with unintentional weight loss associated with dyspeptic symptoms should consult a physician before using Ranitidine 75 mg tablets.

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

Patients with renal impairment (creatinine clearance <50 ml/min) and/or hepatic impairment, or patients undergoing regular medical supervision for other reasons and patients suffering from any other illness or taking medications either physician prescribed or self-prescribed are advised to consult their doctor before using Ranitidine 75 mg tablets.

Ranitidine is excreted via the kidney and so plasma levels of the drug are increased in patients with renal impairment. Therefore, Ranitidine 75 mg tablets are not suitable for these patients without medical supervision. The dosage should be adjusted as detailed above in section 4.2 in Renal impairment.

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).

Regular supervision of patients who are taking non-steroidal anti-inflammatory drugs concomitantly with ranitidine is recommended, especially in in the elderly and in those with a history of peptic ulcer. Current evidence shows that ranitidine protects against NSAID associated ulceration in the duodenum and not in the stomach.

## 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:

At plasma levels such as those that follow the use of standard recommended dosages, ranitidine does not inhibit the hepatic cytochrome P450 oxygenase system. Therefore, at the usual therapeutic dosages, ranitidine does not potentiate the effect of medicines which are inactivated by this enzyme system. These include: 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) Competition for renal tubular secretion:

Since ranitidine is partially eliminated by the cationic system, it may affect the clearance of other drugs eliminated by this route. High doses of ranitidine (e.g. such as those used in the treatment of Zollinger-Ellison syndrome) may reduce the excretion of procainamide and N-acetylprocainamide resulting in increased plasma levels of these drugs.

3) 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, itraconazole, posaconazole, atazanavir, delaviridine, gefitnib) of drugs whose absorption is pH-

dependent. The changes in absorption of these drugs must be taken into account.

If the use of erlotinib is considered during treatment with ranitidine, dosing must be staggered: erlotinib must be administered at least 2 hours before or 10 hours after administration of ranitidine.

After long-term treatment with ranitidine it is possible that absorption of cyanocobalamine may be inhibited, resulting in vitamin B12 deficiency.

Ranitidine may increase the plasma concentrations and effects of alcohol.

There is no evidence of an interaction between ranitidine and amoxicillin and metronidazole.

If anti-acids or high doses (2 g) of sucralfate are administered concurrently with ranitidine, the absorption of ranitidine may be reduced. This effect does not occur if these drugs are taken 2 hours after one another.

## 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 (see section 5.3).

Pregnancy
Ranitidine crosses the placenta. Like other drugs ranitidine should only be used during pregnancy if considered essential.

Lactation
Ranitidine is excreted in human breast milk. Like other drugs ranitidine should only be used during breast-feeding if considered essential.

## 4.7 Effects on ability to drive and use machines

There are inadequate data on the effect of Ranitidine 75 mg tablets on the ability to drive.

## 4.8 Undesirable effects

The following convention is used for the classification of undesirable effects: very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to <1/100), rare (≥ 1/10,000 to <1/1,000), very rare (<1/10,000), not known (cannot be estimated from the available data).
The incidence of adverse events has been determined from spontaneous reports from post-marketing data.

Blood and lymphatic system disorders:

Very rare: changes in blood count (leukopenia, thrombocytopenia). These are usually reversible. Agranulocytosis and pancytopenia, sometimes accompanied by bone marrow hypoplasia or bone marrow aplasia.

Immune system disorders:
Rare: hypersensitivity reactions (urticaria, angioedema, fever, bronchospasms, hypotension and chest pain).
Very rare: anaphylactic shock.
Unknown: dyspnoea
These reactions were observed after a single dose.

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

Nervous system disorders:
Very rare: headache (sometimes severe), dizziness and reversible involuntary movement disorders.

Eye disorders:
Very rare: blurred vision (reversible).

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, AV block and tachycardia.

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, breast symptoms and breast conditions (such as gynaecomastia in men and galactorrhoea).

Paediatric population:
The safety of ranitidine has been evaluated in children aged between 0 and 16 years with acid-related diseases and ranitidine was generally well tolerated with a side effect profile similar to that of adults. There are limited data available on long-term use, in particular relating to 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 professionals 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 overdosage with ranitidine formulations.

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

# 5 PHARMACOLOGICAL PROPERTIES

## 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: H2-receptor antagonist

ATC code A02B A02

Ranitidine is a specific fast-acting histamine $H_2$-receptor antagonist that inhibits both basal and stimulated gastric acid secretion. Ranitidine reduces both the volume of gastric secretion and the hydrogen ion and pepsin concentration. Ranitidine has a long duration of action. A dose of 75 mg provides effective inhibition of gastric acid secretion for up to 12 hours. Clinical studies show that Ranitidine 75 mg tablets give relief from symptoms for a maximum of 12 hours.

## 5.2 Pharmacokinetic properties

The bioavailability of ranitidine after oral administration is approximately 50%. Under normal circumstances, peak plasma concentrations fall within the 236 to 270 ng/ml range and are reached 2 to 3 hours after oral administration of a 75 mg dose. Plasma concentrations of ranitidine are proportional to the dose used up to doses of 300 mg.

Ranitidine is not metabolised in great quantities. Elimination of the drug takes place mainly via tubular secretion. The elimination half-life is 2 to 3 hours.

In excretion balance studies, after administration of 150 mg 3H-ranitidine, 93% of an intravenous dose was excreted in the urine and 5% in the faeces; after oral administration, 60-70% of an oral dose was excreted in the urine and 26% in the faeces. From analysis of urine over 24 hours it appears that 70% of the intravenous dose and 35% of the oral dose is excreted in unchanged form. Ranitidine is metabolised in the same way following oral and intravenous administration: approximately 6% of the dose is excreted in the urine 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

No particulars.

# 6 PHARMACEUTICAL PARTICULARS

## 6.1 List of excipients

**Tablet core:**
Microcrystalline cellulose
Croscarmellose sodium
Anhydrous colloidal silica
Purified talc
Magnesium stearate

**Tablet coating**:
Hypromellose
Castor oil
Titanium dioxide (E171)
Yellow iron oxide (E172)
Purified talc

## 6.2 Incompatibilities

Not applicable.

## 6.3 Shelf life

3 years.

## 6.4 Special precautions for storage

This medicinal product does not require any special storage condition.

## 6.5 Nature and contents of container

Ranitidine 75 mg tablets are packaged in aluminium blister packs of 6 or 10 tablets. The carton contains 6, 10, 12, 24, 30 or 60 tablets. Not all pack sizes may be marketed.

## 6.6 Special precautions for disposal and other handling

No special requirements.

Any unused tablets or waste material should be disposed of in accordance with local requirements.

## 7 MARKETING AUTHORISATION HOLDER

Accord Healthcare Limited
Sage House,
319 Pinner Road,
North Harrow,
Middlesex HA1 4HF,
United Kingdom

## 8 MARKETING AUTHORISATION NUMBER

PA 1390/017/003

## 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of First Authorisation: 15th February 2013

## 10 DATE OF REVISION OF THE TEXT

February 2015