IRISH MEDICINES BOARD ACT 1995, as amended

Medicinal Products (Control of Placing on the Market) Regulations, 2007, as amended

PA0408/029/001
Case No: 2043881

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

Ranbaxy Ireland Limited

Spafield, Cork Road, **Cashel**, **Co. Tipperary**, **Ireland**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

Rimatidine 200mg Film-Coated Tablets

the particulars of which are set out in the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **22/04/2008**.

Signed on behalf of the Irish Medicines Board this

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A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Rimatidine 200mg Film-coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 200mg Cimetidine

Excipients: Each tablet contains 61.48mg of Lactose Monohydrate
For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Film coated tablet (Tablet)

Round, pale green, film-coated tablet embossed ‘RC 200’ on one face and plain on the other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

In the treatment of benign ulceration of oesophagus stomach, upper intestinal tract (including post-operative stomal area) and the Zollinger-Ellison syndrome.
In the management of conditions benefiting from reduced gastric acid secretion.
In the long term maintenance management of benign peptic ulcer disease under regular surveillance.

4.2 Posology and method of administration

For oral administration.

Adults:
The usual dose is 400mg twice a day with breakfast and at bedtime. Alternatively patients with duodenal or benign gastric ulceration may be treated with a single dose of 800mg at bedtime. Regimes of 200mg thrice daily with meals and 400mg nocte or, if in adequate, 400mg q.d.s. with meals and at bedtime may also be used.

In oesophageal reflux 400mg q.d.s. with meals and at bedtime for 4 to 8 weeks is recommended.

In patients with very high gastric acid secretion (e.g. Zollinger-Ellison syndrome) it may be necessary to increase the dose to 400mg q.d.s. or occasionally higher.

Treatment should be given initially for at least 4 weeks (6 weeks in the case of benign ulcer). In patients who may benefit from a reduction of gastric secretion, dosage may be reduced to a maintenance dose of 400mg at bedtime, or in the morning and at bedtime.

A similar maintenance regime may be used to prevent relapse in patients with benign peptic ulceration. Patients on prolonged treatment (particularly those treated for more than one year) should be kept under regular surveillance.

Antacids may be used concurrently if required.

In the prophylaxis of haemorrhage from "stress" ulceration doses up to a maximum of 2.4g daily may be given in

divided doses. 200-400mg doses can be given every 4 to 6 hours by oral, nasogastric or parenteral routes (N.B. by direct intravenous injection a dose of 200mg should not be exceeded - see parenteral dosage recommendations).

In the prophylaxis of acid aspiration (Mendelson's Syndrome) a single dose of 400mg may be given 90-120 minutes before induction of general anaesthesia or, in obstetric practice, at the start of labour. While such a risk persists a dose of up to 400mg may be repeated (parenterally if appropriate) at 4 hourly intervals as required, up to the usual maximum of 2.4g/day.

In pancreatic insufficiency, for protection of pancreatic enzyme supplements, 800-1600mg per day may be given according to response in four divided doses, one to one and a half hours before meals.

The total daily dose by any route should not usually exceed 2400mg.

Dosage should be reduced in patients with impaired renal function when creatinine clearance is below 50ml/minute.

Creatinine Clearance	Daily Dosage
30-50ml/minute	200mg q.d.s.
15-30ml/minute	200mg t.d.s.
0-15ml/minute	200mg b.d.

Cimetidine is removed by haemodialysis, but not to any significant extent by peritoneal dialysis.

Elderly:
The normal adult dosage may be used unless renal function is markedly impaired.

Children:
Experience in children is less than that in adults. In children more than 2 years old, cimetidine 25-30mg/kg body weight/day in divided doses may be administered by either the oral or parenteral routes.

The use of Cimetidine in children less than 2 years old is not fully evaluated.

4.3 Contraindications

No known contra-indications.

4.4 Special warnings and precautions for use

Before initiation of cimetidine therapy, for any gastric ulceration malignancy should be excluded by endoscopy, and biopsy if possible. Treatment with cimetidine can mask the symptoms and assist transient healing of gastric cancer. The consequences of a potential delay in diagnosis should be kept in mind particularly in patients of middle age or over with new or recently changed dyspeptic symptoms.

The safety of prolonged use is not fully established and patients on prolonged treatment (particularly those treated for one year) should be kept under regular surveillance with particular attention to the pathology of the gastrointestinal tract.

In patients on drug treatment or with illnesses which could cause falls in blood cell counts, the possibility that H_2 receptor antagonism could potentiate this effect should be borne in mind.

4.5 Interaction with other medicinal products and other forms of interaction

Cimetidine can prolong the elimination of drugs metabolised by oxidation in the liver. Pharmacological interactions with a number of drugs e.g. diazepam, propranolol, have been demonstrated; only those with oral anticoagulants, phenytoin and theophylline appear to date to be of clinical significance. Close monitoring of patients on cimetidine

receiving oral anticoagulants, phenytoin, theophylline is recommended. A reduction in their dosage may be necessary.

4.6 Pregnancy and lactation

Cimetidine should not be administered during pregnancy or lactation in women breast-feeding infants unless considered essential by the physician. Animal studies of reproduction have shown no drug-related abnormality. Significant levels of drug reach breast milk.

4.7 Effects on ability to drive and use machines

None stated.

4.8 Undesirable effects

Gynaecomastia has been reported with cimetidine. Diarrhoea, dizziness, rash, tiredness have also occurred. Evidence of reversible liver damage has been reported and acute pancreatitis, interstitial nephritis with occasional increases in plasma creatinine, thrombocytopenia, headache, myalgia, arthralgia. Reversible impotence has been reported but no casual relationship established at usual therapeutic doses.

Confusional states, mood and behavioural changes, insomnia, may occur especially in the elderly or in very ill patients or those with renal failure. Those on high dosage are particularly at risk. These states are usually reversible.

4.9 Overdose

Acute overdosage of up to 20g has been reported with no significant ill effects.
Induction of vomiting and/or gastric lavage may be employed together with symptomatic and supportive therapy.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

An H_2-receptor antagonist.

5.2 Pharmacokinetic properties

It is well absorbed after oral dosing, metabolised in the liver and excreted mainly through the kidney with a $T_{1/2}$ of about 3-4 hours. The effects on acid secretion are of longer duration.

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

Lactose monohydrate
Maize Starch
Povidone
Magnesium stearate
Sodium starch glycollate (Type A)

Film coat:
Opadry (Colorcon) OY-5912
(Contains Hypromellose, Titanium Dioxide, Macrogol (400), Quinoline Yellow Aluminium Lake, Iron Oxide Yellow, Indigo Carmine Aluminium Lake)

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

2 years

6.4 Special precautions for storage

Containers, Do not store above 25°C. Store in the original container. Keep the container tightly closed.

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

6.5 Nature and contents of container

White polypropylene containers and polyethylene lids containing 1000, 500, 250 and 100 tablets.

Aluminium/PVC blister packs composed of 120 or 60 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

Ranbaxy Ireland Limited
Spafield
Cork Road
Cashel
County Tipperary
Ireland

8 MARKETING AUTHORISATION NUMBER

PA 408/29/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 22nd April 1993
Date of last renewal: 22nd April 2008

10 DATE OF REVISION OF THE TEXT

June 2010