IRISH MEDICINES BOARD ACTS 1995 AND 2006

MEDICINAL PRODUCTS(CONTROL OF PLACING ON THE MARKET)REGULATIONS,2007

(S.I. No.540 of 2007)

PA0408/004/001
Case No: 2051264

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

Rimadol Paracetamol Tablets BP 500mg

The particulars of which are set out in Part I and Part II of 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 **29/05/2008**.

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

Rimadol Paracetamol Tablets BP 500 mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 500mg of Paracetamol.

Excipients: Each tablet contains 16.67mg lactose monohydrate.

For a full list of excipients see section 6.1

3 PHARMACEUTICAL FORM

Tablet

White, capsule shaped tablet, embossed with 'RIMADOL' on both sides.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

In the management of the symptoms of headache, toothache, common cold, influenza, menstrual pain, musculoskeletal disorders.

4.2 Posology and method of administration

For oral administration.

Adults (including the elderly):

The usual dose is 2 tablets (1000mg) repeated if necessary 3-4 times daily to a maximum of 8 tablets in any 24 hour period.

Children aged 6-12 years:

The usual dose is half to one tablet (250-500mg) repeated if necessary 3-4 times daily to a maximum of 4 tablets in any 24 hour period.

Rimadol Paracetamol Tablets are not suitable for children under 6 years of age.

These doses should not be repeated more frequently than every 4 hours and not more than 4 doses should be given in any 24 hour period.

4.3 Contraindications

Hypersensitivity to paracetomal or any of the other constituents.
Use in children under 6 years of age.

4.4 Special warnings and precautions for use

Caution is advised in the administration of paracetamol to patients with severe renal or severe hepatic impairment. The hazard of overdose is greater in those with moderate and severe liver disease.
Prolonged use except under medical supervision may be harmful.
Do not exceed the stated dose.
If symptoms persist, consult the physician.
Keep out of reach of children.
Patients should be advised not to take other paracetamol-containing products concurrently.
This product should only be used when clearly necessary.
Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

The speed of absorption of paracetamol may be increased by metoclopramide or domperidone and absorption reduced by cholestyramine. The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular daily use of paracetamol with increased risk of bleeding; occasional doses have no significant effect.

4.6 Pregnancy and lactation

There is epidemiological evidence of the safety of Paracetamol in pregnancy. Paracetamol is the mild analgesic of choice during pregnancy, however as with all drugs, caution should be exercised in its use during the first trimester. Paracetamol is excreted in breast milk. However, the level of paracetamol present is not considered to be harmful.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

Side effects are rare and usually mild, though haematological reactions including thrombocytopenia, leucopenia, pancytopenia, neutropenia and agranulocytosis have been reported. Skin rashes and other hypersensitivity reactions occur occasionally.

4.9 Overdose

Immediate medical attention (in-hospital, if possible) is required in the event of overdose, even if there are no significant early symptoms. There may be no early symptoms following a life-threatening overdose.
Ingestion of more than 12g paracetemol (24 standard 500mg tablets) or more than 150mg paracetamol per kg bodyweight (9g paracetomal in a 50kg individual), whichever is the smaller, can cause severe liver damage.
Liver damage (as demonstrated by a rise in plasma transaminase levels) may be apparent between 8 and 36 hours following overdose.
Biochemical evidence of maximal damage, however, may not be attained until 72-96 hours after ingestion of the overdose.

Intravenous N-acetylcysteine (NAC) is effective when initiated within 8 hours of the overdose. Efficacy declines progressively after this time, but NAC may provide some benefit up to and possibly beyond 24 hours. Oral methionine is also effective provided that it is given within 10 to 12 hours of the overdose. Activated charcoal should be considered if the dose of paracetamol ingested exceeds 12g or 150mg/kg, whichever is the smaller, and the procedure can be undertaken within 1 hour of the overdose. There is little evidence that undertaking gastric lavage will be of benefit to a patient in whom paracetamol is known to have been the only substance ingested.

Symptoms of paraceetamol overdose in the first 24 hours may include pallor, nausea, vomiting, anorexia, and

abdominal pain. Abnormalities of glucose metabolism and metabolic acidosis may occur. In severe poisoning, hepatic failure may progress to encephalopathy, coma and death. Liver damage results when excess quantities of a toxic metabolite (usually adequately detoxified by glutathione when normal doses of paracetamol are ingested) become irreversibly bound to liver tissue. Acute renal failure with acute tubular necrosis may develop even in the absence of severe liver damage. Cardiac arrhythmias and pancreatitis have been reported.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Paracetamol has analgesic and anti-pyretic effects but has only weak anti-inflammatory effects. These actions are considered to be due to inhibition of the biosynthesis of prostaglandins.

5.2 Pharmacokinetic properties

Paracetamol is readily absorbed from the gastro-intestinal tract with peak plasma concentrations occurring about 30 minutes to 2 hours after ingestion. It is metabolised in the liver and excreted in the urine mainly as the glucuronide and sulphate conjugates. Less than 5% is excreted as unchanged Paracetamol. The elimination half life varies from 1-4 hours.

Plasma protein binding is negligible at usual therapeutic concentrations but increases with increasing concentrations. A minor hydroxylated metabolite which is usually produced in very small amounts by mixed function oxidizes in the liver and which is usually detoxified by conjugation with liver glutathione may accumulate following Paracetamol overdosage and cause liver damage.

Practically no Paracetamol is excreted unchanged, and the bulk is excreted after hepatic conjugation with glycuronic acid (about 60%), sulphuric acid (about 35%) or cysteine (3%).

Children have less capacity for glycuronidation of the drug than do adults. When high doses are ingested Paracetamol undergoes N-Hydroxylation to form N-Acetyl Benzo-Quinoneimine, a highly reactive intermediate. This metabolite reacts with Sulfhydryl groups in proteins and glutathione. When hepatic glutathione is depleted reaction with hepatic proteins is increased and hepatic necrosis is the result. A review of the absorption and fate and bioavailability of Paracetamol was carried out by Hunt et Al.

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

Maize Starch
Lactose Monohydrate
Povidone (K30)
Magnesium Stearate
Sodium Starch Glycolate
Colloidal Anhydrous Silica

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

3 years.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

White polypropylene containers with tamper evident polyethylene closures.
Pack sizes: 25, 50, 100, 500, 1000 and 5000.

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 Ltd
Spafield
Cork Road
Cashel
Co. Tipperary
Ireland

8 MARKETING AUTHORISATION NUMBER

PA 408/4/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 09 April 1987
Date of last renewal: 09 April 2007

10 DATE OF REVISION OF THE TEXT

July 2007