SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

RECTOL 250 (Acetaminophen Suppositories USP 250 mg)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each suppository contains.

Acetaminophen (Paracetmol) USP 250 mg

Excipients qs

Colour : Titanium Dioxide BP

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Suppositories

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the treatment of mild to moderate pain and pyrexia in children:

Paracetamol Suppositories is indicated in children aged 1 to 5 years.

Paracetamol Suppositories may be especially useful in patients unable to take oral forms of paracetamol, e.g. post-operatively or with nausea and vomiting

4.2 Posology and method of administration

Posology

Children 1 to 5 years (125 mg suppositories)

The dosage should be based on age and weight i.e.

1 year (10 Kg) - 125mg (1 suppository)

5 years (20 Kg) - 250mg (2 suppositories)

Method of administration

These doses may be repeated up to a maximum of 4 times in 24 hours. The dose should not be repeated more frequently than every 4 hours. The recommended dose should not be exceeded. Higher doses do not produce any increase in analgesic effect.

Only whole suppositories should be administered – do not break suppository before administration.

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4.3 Contraindications

Hypersensitivity to Clotrimazole or any ingredient in this medicine.

4.4 Special warnings and precautions

Rectol – 250 suppositories should not be combined with other analgesic medications that contain paracetamol. Paracetamol should be given with care to patients with impaired kidney or liver function.

Doses higher than those recommended involve a risk of very severe liver damage. Liver damage is also associated with certain risk factors (see also Section 4.5 Interaction with other medicinal products and other forms of interaction, and Section 4.9 Overdose). If liver damage is suspected then liver function tests should be performed.

Do not exceed the recommended dose. If symptoms persist consult your doctor. Keep out of the sight and reach of children.

Caution is advised if paracetamol is administered concomitantly with flucloxacillin due to increased risk of high anion gap metabolic acidosis (HAGMA), particularly in patients with severe renal impairment, sepsis, malnutrition and other sources of glutathione deficiency (e.g. chronic alcoholism), as well as those using maximum daily doses of paracetamol.

Close monitoring, including measurement of urinary 5-oxoproline, is recommended

4.5 Interaction with other medicinal products and other form of interactions:

Drugs which induce hepatic microsomal enzymes such as alcohol, barbiturates and other anticonvulsants, may increase the hepatotoxicity of paracetamol, particularly after overdosage.

The anti-coagulant effect of warfarin and other coumarins may be enhanced by prolonged regular use of paracetamol with increased risk of bleeding.

The effect appears to increase as the dose of paracetamol is increased, but can occur with doses as low as 1.5–2 g paracetamol per day for at least 5–7 days. Occasional doses have no significant effect.

Probenicid inhibits the glucuronidation of paracetamol which can affect the clearance of paracetamol. This should be considered when these medicines are administered concomitantly.

Caution should be taken when paracetamol is used concomitantly with flucloxacillin as concurrent intake has been associated with high anion gap metabolic acidosis, especially in patients with risks factors (see section 4.4)

Paracetamol may affect the pharmacokinetics of chloramphenicol. This interaction should be considered when these medications are administered concomitantly, especially in malnourished patients.

Enzyme-inducing medicines, such as some antiepileptic drugs (phenytoin, phenobarbital, carbamazepine, primidone) have been shown in pharmacokinetic studies to reduce the plasma AUC of paracetamol to approx. 60 %. Other substances with enzyme-inducing properties, e.g. rifampicin and St. John's wort (hypericum) are also suspected of causing lowered concentrations of paracetamol. In addition, the risk of liver damage during treatment with maximum recommended doses of paracetamol will be higher in patients being treated with enzyme-inducing agents.

4.6 Pregnancy and Lactation

A large amount of data on pregnant women indicate neither malformative, nor feto/neonatal toxicity. Epidemiological studies on neurodevelopment in children exposed to paracetamol in utero show inconclusive results. If clinically needed, paracetamol can be used during pregnancy however it should be used at the lowest effective dose for the shortest possible time and at the lowest possible frequency.

Paracetamol is excreted in breast milk but not in clinically significant amounts.

Available published data do not contraindicate breast-feeding

4.7 Effects on Ability to Drive and Use Machines

None.

4.8 Undesirable effects:

Side-effects at therapeutic doses are rare

Frequency	**System Organ Class (SOC)**	**Event**
Common (≥1/100 to <1/10)	Gastrointestinal disorders	Redness of the rectal mucous membranes

Rare	Immune system disorders	Allergic reaction
(≥1/10,000 to <1/1,000)	Hepatobiliary disorders	Liver damage
	Skin and subcutaneous tissue	Exanthema, urticaria, angioedema
	Disorders	Increase in creatinine
	Investigations	(mostly secondary to hepatorenal syndrome)

Very rare cases of serious skin reactions have been reported.

There have been reports of blood dyscrasias including thromocytopenia and agranulocytosis, but these were not necessarily causally related to paracetamol.

Hepatic necrosis may occur after overdosage.

4.9 Overdose

Toxicity

Liver damage is possible in adults who have taken 10g or more of paracetamol. Ingestion of 5g or more of paracetamol may lead to liver damage if the patient has risk factors (see below).

Risk factors

If the patient

- Is on long term treatment with carabamazepine, phenobarbitone, phenytoin, primidone, rifampicin, St John's Wort or other drugs that induce liver enzymes.

Or

- Is likely to be glutathione deplete e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia.

Symptoms

Symptoms of paracetamol overdosage in the first 24 hours are pallor, nausea, vomiting, anorexia and abdominal pain. Liver damage may become apparent 12 to 48 hours after administration and clinical symptoms generally culminate after 4 to 6 days. Abnormalities of glucose metabolism and metabolic acidosis may occur.

In severe poisoning, hepatic failure may progress to encephalopathy, haemorrhage, hypoglycaemia, cerebral oedema, and death. Acute renal failure with acute tubular necrosis, strongly suggested by loin pain, haematuria and proteinuria, may develop even in the absence of severe liver damage. Cardiac arrhythmias and pancreatitis have been reported

Management

Immediate treatment is essential in the management of paracetamol overdose.

Despite a lack of clinically significant early symptoms, patients should be referred urgently to hospital for immediate medical attention. This is because early symptoms may be limited to nausea or vomiting and may not reflect the severity of overdose or the risk of organ damage. Management should be in accordance with established treatment guidelines.

As concentrations soon after paracetamol ingestion are unreliable, plasma paracetamol concentration should be measured at 4 hours or later after the initial administration. Treatment with N-acetylcysteine may be used for up to 24 hours after administration of paracetamol; however, the maximum protective effect is only obtained up to 8 hours post-administration. The effectiveness of this antidote declines sharply after this 8 hour time period. If required, the patient should be given intravenous N-acetylcysteine, in line with the established dosage schedule. If vomiting is not a problem, then oral methionine may be a suitable alternative for remote areas, outside hospital.

Management of those patients presenting with serious hepatic dysfunction 24 hours after paracetamol administration should be discussed with the National Poisons Information Centre (NPIS) or a liver unit.

5. PHARMACOLOGICAL PROPERTIES:

5.1 Pharmacodynamic properties:

Analgesic, Antipyretic ATC Code: N02 BE01

Paracetamol is an aniline derivative with analgesic and antipyretic actions similar to those of aspirin but with no demonstrable anti-inflammatory activity. Paracetamol is less irritant to the stomach than aspirin. It does not affect thrombocyte aggregation or bleeding time. Paracetamol is generally well tolerated by patients hypersensitive to acetylsalicylic acid

5.2 Pharmacokinetic properties:

Absorption

Paracetamol is well absorbed by both oral and rectal routes. Peak plasma concentrations occur about 2 to 3 hours after rectal administration. The plasma half life is about 2 hours.

Biotransformation

Paracetamol is primarily metabolised in the liver by conjugation to glucuronide and sulphate. A small amount (about 3-10% of a therapeutic dose) is metabolised by oxidation and the reactive intermediate metabolite thus formed is bound preferentially to the liver glutathione and excreted as cysteine and mercapturic acid conjugates.

Elimination

Excretion occurs via the kidneys. 2-3% of a therapeutic dose is excreted unchanged; 80-90% as glucuronide and sulphate and a smaller amount as cystein and mercapturic acid derivatives

5.3 Preclinical safety data

Conventional studies using the currently accepted standards for the evaluation of toxicity to reproduction and development are not available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Macrogols 1500 BP, Macrogols 6000 BP, Methyl Hydroxybenzoate BP,Propyl Hydroxybenzoate ,Butylated Hydroxytoluene BP, Titanium Dioxide BP

6.2 Incompatibilities

Not known

6.3 Shelf Life

36 months

6.4 Special precaution for storage

Store in original package below 30^0C.

6.5 Nature and content of container

Paracetamol suppositories pack in polyvinylchloride foil coated with Polyethylene. (PVC-PE Foil), Two strips each containing 5 Suppositories are packed in a carton along with pack insert..

7. MARKETING AUTHORIZATION HOLDER

BLISS GVS PHARMA LTD.,
102, Hyde Park, Saki-Vihar road,
Andheri (East) Mumbai 400 072
INDIA.

8. NUMBER(S) IN THE NATIONAL REGISTER OF FINISHED PHARMACEUTICAL PRODUCTS

Registration number: 04960/07158/REN/2019

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORIZATION

04.02.2020

10. DATE OF REVISION OF THE TEXT

July 2023