

1. NAME OF THE MEDICINAL PRODUCT

Parasum Suppositories 125 mg and 250 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each suppository contains:

Paracetamol BP 125 mg

Each suppository contains:

Paracetamol BP 250 mg

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

White to off white color torpedo shape suppositories.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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

Parasum 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

For rectal use only.

The dosage should be based on age and weight:

Parasum 125 mg Suppository

Children 1 to 5 years

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

1 years (10 Kg) 125 mg (1 suppository)

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

Parasum 250 mg Suppository

Children 6 to 12 years

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

6 years (20 Kg) 250 mg (1 suppository)

12 years (40 Kg) 500 mg (2 suppositories)

Method of administration

This dose 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.

The product should not be used for more than 3 days, except on the advice of a doctor. Higher doses do not produce any increase in analgesic effect. Only whole suppositories should be administered– do not break suppository before administration.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Parasum 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.

Label and Leaflet will state the following warnings:

Label:

“Immediate medical advice should be sought in the event of an overdose, even if the child seems well”.

“Do not give with any other paracetamol containing products.”

Leaflet:

“Immediate medical advice should be sought in the event of an overdose, even if the child seems well, because of the risk of delayed, serious liver damage.”

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 forms of interaction

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

The anticoagulant 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.

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.

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 risk factors.

4.6 Fertility, pregnancy and lactation

Pregnancy: Parasum Suppositories can be used during pregnancy if clinically needed.

Lactation: Parasum Suppositories can be used during breast feeding.

4.7 Effects on ability to drive and use machines

None known

4.8 Undesirable effects

Side-effects at therapeutic doses are rare.

Frequency	System organ class (SOC)	Event
Common ($\geq 1/100$ to $< 1/10$)	Gastrointestinal disorders	Redness of the rectal mucous membrane
Rare ($\geq 1/10,000$ to $< 1/1,000$)	Immune system disorder	Allergic reaction
Rare ($\geq 1/10,000$ to $< 1/1,000$)	Hepatobiliary disorder	Liver damage
Rare ($\geq 1/10,000$ to $< 1/1,000$)	Skin and subcutaneous tissue disorders	Exanthema, urticaria, angiodema
Rare ($\geq 1/10,000$ to $< 1/1,000$)	Investigations	Increase in creatinine (mostly secondary to hepatorenal syndrome)

Very rare cases of serious skin reactions have been reported.

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

Hepatic necrosis may occur after overdose.

“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 the TMDA ADR reporting tool; website: <https://imis.tmda.go.tz/artt> or search for TMDA Adverse Reactions Reporting Tool in the Google Play Store”.

4.9 Overdose

Toxicity

Liver damage is possible in adults who have taken 10 g or more of paracetamol. Ingestion of 5 g 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 carbamazepine, phenobarbitone, phenytoin, primidone, rifampicin, St John's wort or other drugs that induce liver enzymes,

Or

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

Symptoms

Symptoms of paracetamol overdose 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 see BNF overdose section.

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

Pharmacotherapeutic group: Other analgesics and antipyretics, Anilides.

ATC Code: N02BE01

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 310% 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 cystein and mercapturic acid conjugates.

Elimination

Excretion occurs via the kidneys. 23% 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

Non-clinical data reveal 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**

Hard fat

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Do not store above 30°C, store in dry place. Do not freeze.
Keep all medicines out of reach of children.

6.5 Nature and contents of container

5 Rectal suppositories are packed in PVC/PE strip and 2 such strips of 5 suppositories are packed in a carton along with pack insert.

6.6 Special precautions for disposal and other handling

None

7. MARKETING AUTHORISATION HOLDER

Kusum Healthcare Pvt. Ltd.

SP-289(A), RIICO Industrial Area, Chopanki, Bhiwadi, Dist. Alwar (Rajasthan) India

8. MARKETING AUTHORISATION NUMBER(S)

TAN 21 HM 0312

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORIZATION

2021-08-20

10. DATE OF REVISION OF THE TEXT

11. LEGAL CATEGORY

Prescription only medicine