SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Paraserts 1000mg Suppositories

Paracetamol 1000mg Suppositories

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each suppository contains paracetamol 1000 mg.

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 such as toothache and/or pyrexia. Paraserts/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

Method of administration: Rectal

Adults

1 suppository every 4 to 6 hours up to a maximum of 4 suppositories 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. The product should not be used for more than 3 days, except on the advice of a doctor. Only whole suppositories should be administered – do not break suppository before administration

4.3 Contraindications

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

4.4 Special warnings and precautions for use

Paraserts/Paracetamol 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.

In general, the habitual use of painkillers, especially with combinations of more than one pain killing active ingredient, can lead to permanent kidney damage with the risk of liver failure (analgesic nephropathy).

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."

Cases of high anion gap metabolic acidosis (HAGMA) due to pyroglutamic acidosis have been reported in patients with severe illness such as severe renal impairment and sepsis, or in patients with malnutrition or other sources of glutathione deficiency (e.g. chronic alcoholism) who were treated with paracetamol at therapeutic dose for a prolonged period or a combination of paracetamol and flucloxacillin. If HAGMA due to pyroglutamic acidosis is suspected, prompt discontinuation of paracetamol and close monitoring is recommended. The measurement of urinary 5-oxoproline may be useful to identify pyroglutamic acidosis as underlying cause of HAGMA in patients with multiple risk factors.

4.5 Interaction with other medicinal products and other forms of interaction

The absorption of paracetamol is speeded by metaclopramide or domperidone, and absorption is reduced by colestyramine.

The anticoagulant effect of warfarin and other coumarins may be increased by long term regular daily use of paracetamol, with increased risk of bleeding. Occasional doses of paracetamol do not have a significant effect on these anticoagulants.

Enzyme-inducing medicines, such as some antiepileptic drugs (phenytoin, phenobarbital, carbamazepine) 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 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 due to pyroglutamic acidosis, especially in patients with risk factors (see section 4.4).

4.6 Fertility, 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 known.

4.8 Undesirable effects

Common >1/100	*Miscellaneous:*	Redness of the rectal mucous membranes
Rare <1/1000	*General:* *Skin:* *Liver:*	Allergic reactions including skin rashes Exanthema, urticaria Liver damage

	Genitourinary:	Increase in creatinine (mostly secondary to hepatorenal syndrome)
Not Known (cannot be estimated from the available data)	*Metabolism and nutrition disorders:*	High anion gap metabolic acidosis

There have been some reports of blood dyscrasias including thrombocytopenia and argranulocytosis, with the use of paracetamol- containing products, but the causal relationship has not been established.

Description of selected adverse reactions

High anion gap metabolic acidosis

Cases of high anion gap metabolic acidosis due to pyroglutamic acidosis have been observed in patients with risk factors using paracetamol (see section 4.4). Pyroglutamic acidosis may occur as a consequence of low glutathione levels in these patients.

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 the Yellow Card Scheme at www.mhra.go.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

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).

It is considered that excess quantities of a toxic metabolite (usually adequately detoxified by glutathione when normal doses of paracetamol are ingested) become irreversibly bound to liver tissue.

Risk Factors:

If the patient

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

Or

b. Regularly consumes ethanol in excess of recommended amounts

Or

c. 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 ingestion. 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 in the absence of severe liver damage. Cardiac arrythmias and pancreatitis have been reported.

Management:

Immediate treatment is essential in the management of paracetamol overdose. Despite a lack of significant early symptoms, patients should be referred to hospital urgently for immediate medical attention. 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.

Treatment with activated charcoal should be considered if the overdose has been taken by mouth within 1 hour. Plasma paracetamol concentration should be measured at 4 hours or later after ingestion (earlier concentrations are unreliable). Treatment with N-acetylcysteine may

be used up to 24 hours after ingestion of paracetamol, however, the maximum protective effect is obtained up to 8 hours post-ingestion. The effectiveness of the antidote declines sharply after this time. If required the patient should be given intravenous N-acetylcysteine, in line with the established dosage schedule. If vomiting is not a problem, oral methionine may be a suitable alternative for remote areas, outside hospital.

Management of patients who present with serious hepatic dysfunction beyond 24h from ingestion should be discussed with NPIS or a liver unit.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Anilides, 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. It does not affect thrombocyte aggregation or bleeding time. Paracetamol is generally well tolerated by patients hypersensitive to acetylsalicylic acid. It produces analgesia by elevation of the pain threshold and antipyresis through action on the hypothalamic heat-regulation centre.

5.2 Pharmacokinetic properties

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 ¼ hours and is prolonged in cirrhosis.

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 cystein and mercapturic acid conjugates. 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 cysteine 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

Hydrogenated fat

Soyabean Lecithin

6.2 Incompatibilities

None relevant

6.3 Shelf life

36 months

6.4 Special precautions for storage

Do not store above 30ºC

6.5 Nature and contents of container

PVC-Blister packet

In pack size of 10 suppositories

6.6 Special precautions for disposal

None

7 MARKETING AUTHORISATION HOLDER

Amdeepcha Limited
85 Yarmouth Road, Blofield,

Norwich, Norfolk
NR13 4LQ, UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 19255/0013

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

02/11/2011

10 DATE OF REVISION OF THE TEXT

08/01/2025

11 DOSIMETRY (IF APPLICABLE)

Not Applicable

12 INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS (IF APPLICABLE)

Not Applicable