1. Name of the medicinal product

Panalex Suppositories 125mg

Panalex Suppositories 250 mg

2. Qualitative and quantitative composition

Panalex Suppositories 125 mg: Each suppository contains Paracetamol 125 mg.

Panalex Suppositories 250 mg: Each suppository contains Paracetamol 250 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 and pyrexia in children:

Panalex 125 mg is indicated in children aged 1 to 5 years.

Panalex 250 mg is indicated in children aged 6 to 12 years.

Panalex 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)

Children 6 to 12 years (250 mg suppositories)

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

6 years (20 Kg)	-	250mg (1 suppository)
12 years (40 Kg)	-	500mg (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.

4.3 Contraindications
Hypersensitivity to paracetamol or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use
Panalex 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.

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 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.

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 Fertility, pregnancy and lactation
A large amount of data on pregnant women indicates neither malformities, 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
Not relevant.

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 (≥1/10,000 to <1/1,000)	Immune system disorders	Allergic reaction
	Hepatobiliary disorders	Liver damage
	Skin and subcutaneous tissue disorders	Exanthema, urticaria, angioedema
	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 overdosage (see below).

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.

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 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 - 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: 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 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 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
Polyethylene Glycol 1500 BP & polyethylene Glycol 6000 BP

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
36 months.

6.4 Special precautions for storage
Do not store above 30°C.

6.5 Nature and contents of container
PVC/polyethylene blister strips each containing 5 suppositories. Packs of 10 suppositories.

6.6 Special precautions for disposal and other handling
Peel the wrapper apart to remove the suppository, gently push into the rectum pointed end first.

7. Marketing authorisation holder
London United exports Ltd
38 Watford Way
London NW4 3AL

8. Manufacturer

Meridian Enterprises PVT Ltd
Nariman Point
Maharashtra India

9. Date of revision of the text
May 2020