December 2023

SUMMARY OF PRODUCT CHARACTERISTIC (SPC)

1. NAME OF THE MEDICINAL PRODUCT

Adol (Paracetamol 500 mg suppository.)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each suppository contains 500.00 mg paracetamol

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suppositories

Smooth, white to off-white, torpedo shaped suppository.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of mild to moderate pain and fever.
Adol 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

Posology
1 year – 5 years: 1-2 suppositories every 4 to 6 hours
Dosages should be based on the child's age and weight i.e.

- 1 year (10kg) – 125mg (1 suppository)
- 5 years (20kg) – 250mg (2 suppositories)

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. 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 the suppository before administration.

4.3 Contraindications

Hypersensitivity to either paracetamol or any of the other ingredients listed in section 6.1.

4.4 Special warnings and precautions for use

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."

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

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.
Phenytoin may reduce the analgesic and antipyretic effects of paracetamol and may increase the formation of the toxic N-acetyl-p-benzoquinone imine (NAPQI) metabolite of paracetamol leading to increased risk of hepatotoxicity.
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 (see section 4.4).

4.6 Fertility, pregnancy and lactation

Epidemiological studies in human pregnancy have shown no ill effects due to paracetamol used in the recommended dosage, but patients should follow the advice of their doctor regarding its use.
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:*	Allergic reactions including skin rashes
	Skin:	Exanthema, urticaria
	Liver:	Liver damage
	Genitourinary:	Increase in creatinine (mostly secondary to hepatorenal syndrome)

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.

Healthcare professionals are asked to report any suspected adverse reactions via:

Pharmacovigilance and Medical Device Section
Drug Department - U.A.E M.O.H
Hotline: 80011111
Email: pv@mohap.gov.ae
P.O. Box: 1853 Dubai U.A.E.

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 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 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: N02BE01

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 cystein and mercapturic acid derivatives.

5.3 Preclinical safety data

Paracetamol crosses the placenta.
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

Semi-synthetic glycerides of saturated fatty acids from C_8 to C_{18} (Suppocire AM)

6.2 Incompatibilities

None relevant

6.3 Shelf life

60 months

6.4 Special precautions for storage

Store below 30°C, in the original container, protected from heat.

6.5 Nature and contents of container

- **Pack of 10 Suppositories:** 5 Suppositories in a PVC-PE film strip, 2 strips packed in a printed carton along with a leaflet.
- **Pack of 100 Suppositories:** 5 Suppositories in a PVC-PE film strip, 20 strips packed in a printed carton along with a leaflet.

6.6 Special precautions for disposal and other handling

Peel the wrapper apart to remove the suppository, gently pushes into the rectum pointed end first.

7. MARKETING AUTHORISATION HOLDER

Gulf Pharmaceutical Industries - Julphar
Digdaga, Airport Street
Ras Al Khaimah - United Arab Emirates
P.O. Box 997
Tel. No.: (9717) 2 461 461
Fax No.: (9717) 2 462 462

8. MARKETING AUTHORISATION NUMBER(S)

08516/VAR/2023

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Nov 23, 2023

10. DATE OF REVISION OF THE TEXT

22. February. 2023