SUPRAMOL 500 SUPPOSITORIES

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

SUPRAMOL 500 SUPPOSITORIES

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each suppository contains 500mg Paracetamol

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Suppository

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Analgesic and Antipyretic.

4.2 Posology and method of administration

Posology

Adults and children above the age of 12:

1-2 suppositories every 4-6 hours as needed.

Up to 8 suppositories per day.

Method of administration

For rectal use only.

4.3 Contraindications

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

Not to be used in case of sever liver disease.

4.4 4.5 Special warnings and precautions for use

SUPRAMOL 500 suppositories should not be combined with other analgesic medications that contain paracetamol.

Paracetamol may cause liver damage in the following cases: When administered at a higher dosage than recommended, when administered for an extended period, when consuming alcoholic beverages during the treatment period, when taking additional medicines that affect the liver, when suffering from chronic malnutrition.

SUPRAMOL 500 suppositories should be administered with care to patients with impaired kidney or liver function.

The hazards of overdose are greater in those with non-cirrhotic liver disease.

Patients should be informed about the signs of serious skin reactions and use of the drug should be discontinued at the first appearance of skin rash or any other sign of hypersensitivity.

These skin reactions, known as Stevens Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN), and acute generalized exanthematous pustulosis (AGEP), can be fatal.

Reddening of the skin, rash, blisters, and detachment of the upper surface of the skin can occur with the use of drug products that contain paracetamol.

These reactions can occur with first-time use of paracetamol or at any time while it is being taken.

Anyone who develops a skin rash or reaction while using paracetamol should stop the drug and seek medical attention right away.

Anyone who has experienced a serious skin reaction with paracetamol should not take the drug again and should contact their health care professional to discuss alternative pain relievers/fever reducers.

Health care professionals should be aware of this rare risk and consider paracetamol along with other drugs already known to have such an association, when assessing patients with potentially drug induced skin reactions.

Paracetamol can cause accidental poisoning in toddlers and infants. Paracetamol-containing products should be kept well out of reach of children.

Potentially fatal hepatotoxicity can result from paracetamol overdosage.

However, in rare cases, hepatotoxicity has occurred in patients receiving high or excessive doses within therapeutic doses.

Certain patients may be more susceptible to paracetamol hepatotoxicity, e.g., chronic alcoholics, patients with liver disease, or those who are malnourished or taking other drugs that induce hepatic enzymes. Because of the risk of hepatotoxicity, patients should be cautioned against the inadvertent administration of excessive doses of paracetamol by using multiple paracetamol-containing products at once, such as cough and cold remedies, analgesics or arthritic formulations, antipyretics or products for relief of menstrual symptoms or muscle spasm.

Administration of paracetamol to children may be especially prone to error due to the many concentrations and strengths of products available. To avoid dosing errors, all product labels should be checked carefully to ensure calculation of the amount of paracetamol to be given.

Immediate medical advice should be sought in the event of an overdose, because of the risk of delayed, serious liver damage.

The stated dose of this medicine should not be exceeded when fasting.

Leave at least 4 hours between doses.

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 anti-coagulant effect of warfarin and other coumarins may be enhanced by prolonged regular use of paracetamol with increased risk of bleeding. Occasional doses have no significant effect.

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

Chronic ingestion of anticonvulsants or oral steroid contraceptives induce liver enzymes and may prevent attainment of therapeutic paracetamol levels by increasing first pass metabolism or clearance.

Alcohol can increase the hepatotoxicity of paracetamol overdosage and may have contributed to the acute pancreatitis reported in one patient who had taken an overdose of paracetamol.

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)

Rifampicin

Isoniazid, zidovudine

Non-steroidal anti-inflammatory preparations

Metoclopramide or domperidone - The speed of absorption of paracetamol may be increased

Chloramphenicol

Probenecid

Cholestyramine - absorption is reduced

Other analgesic or antipyretics

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.

When given to the mother in therapeutic doses (1 g single dose), paracetamol crosses the placenta into foetal circulation as early as 30 minutes after ingestion and is metabolised in the foetus by conjugation with sulfate and increasingly with glutathione.

Breastfeeding

Paracetamol is excreted in breast milk but not in a clinically significant amount. Available published data do not contraindicate breast feeding.

Fertility

There is no information relating to the effects of this medicine on fertility.

4.7 Effects on ability to drive and use machines

No adverse effects known.

4.8 Undesirable effects

Adverse drug reactions are rare.

The medicine should be discontinued immediately if:

Sever allergic reactions occur, such as rash and itching, swelling of the face, lips, tongue, throat and/or limbs that can cause breathing or swallowing difficulties.

Severe skin symptoms and skin diseases appear- redness, rash, blisters (rare), can appear also with patients that used paracetamol in the past without any problem.

Vomiting, sudden loss of weight, loss of appetite and yellowing of the skin and eyes starts.

Common ≥1/100 to <1/10

Gastrointestinal disorders- Redness or soreness of the rectal mucous membrane

Rare ≥1/10,000 to <1/1,000

Immune system disorders - Allergic reactions

Hepatobiliary disorders- Liver damage

Skin and subcutaneous tissue disorders - Exanthema, urticaria, angioedema,

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 paracetamol overdose (see Section 4.9).

Nausea, vomiting, constipation.

Lung damage.

Shortness of breath.

Headache.

Restlessness.

Very Rare < 1/10,000

Unregular fatigue, unexpected bruises or bleeding, tendency for more infections (like; a cold)

Chronic hepatic necrosis has been reported in a patient who took daily therapeutic doses of paracetamol for about a year and liver damage has been reported after daily ingestion of excessive amounts for shorter periods. A review of a group of patients with chronic active hepatitis failed to reveal differences in the abnormalities of liver function in those who were

long-term users of paracetamol nor was the control of their disease improved after paracetamol withdrawal.

Side effects can be reported to the Ministry of Health by clicking on the link “Report Side Effects of Drug Treatment” found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link:
https://sideeffects.health.gov.il

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

a. Is on long term treatment with carabamazepine, 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 and clinical symptoms generally culminate after 4-6 days. Abnormalities of glucose metabolism and metabolic acidosis may occur. In severe poisoning, hepatic failure may progress to encephalopathy, coma and death. Acute renal failure with acute tubular necrosis 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 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 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 Nacetylcysteine, 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 the 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 center.

5.2 Pharmacokinetic properties

Absorption

Paracetamol is rapidly and almost completely absorbed from the gastrointestinal tract. Peak plasma concentrations occur about 2 to 3 hours after rectal administration. Usual analgesic doses produce total serum concentrations of 5 to 20mcg/ml.

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 cystein and mercapturic acid conjugates.

Elimination

Paracetamol is excreted in the urine mostly as metabolites; 2-4% is excreted unchanged. The average elimination half life is 1 to 4 hours; half life is slightly prolonged in neonates (2.2 to 5 hours) and in cirrhotics.

The overall elimination rate constant for paracetamol in children, from birth to 12 years of age, is the same as for adults but neonates have diminished capacity to form glucuronide conjugates of paracetamol.

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

In addition to the active ingredient, the medicine also contains: Witepsol

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials

6.4 Special precautions for storage

Do not store above 25^0C. Store in the original package

6.5 Nature and contents of container

Oval milky-white suppository.

The suppositories are provided in aluminum trays in packs of 20 suppositories.

6.6 Special precautions for disposal

The suppository should only be removed from the blister packaging immediately before use.

7. MARKETING AUTHORISATION HOLDER

Sam-On Ltd.

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Bat-Yam 59602

8. MARKETING AUTHORISATION NUMBER

350325647

9. DATE OF REVISION OF THE TEXT

2/2025

SPMC rev date	Revised chapters	Reference for update	Remarks
2/2025	NEW	Paracetamol 500mg Suppositories SmPC – MHRA 5/2022	First SMPC addition.