FEBRAMOL

Suppositories & Syrup

Composition

Febramol 150 Suppositories
Each suppository contains Paracetamol 150 mg.

Febramol 300 Suppositories
Each suppository contains Paracetamol 300 mg.

Febramol Syrup
Each teaspoonful (5 ml) contains Paracetamol 125 mg.

Action

Paracetamol is a para-aminophenol derivative that exhibits analgesic and anti–pyretic activity. Its mechanism of action is believed to include inhibition of prostaglandin synthesis, primarily within the central nervous system. It is given by mouth or rectally (suppositories) for mild to moderate pain and fever.

The lack of peripheral prostaglandin inhibition confers important pharmacological properties such as the maintenance of the protective prostaglandins within the gastrointestinal tract. Paracetamol is, therefore, particularly suitable for patients with a history of disease or on concomitant medication, where peripheral prostaglandin inhibition would be undesirable (such as, for example, those with a history of gastrointestinal bleeding or the elderly).

Pharmacokinetics

Absorption
Paracetamol is rapidly and almost completely absorbed from the gastrointestinal tract. Food intake delays paracetamol absorption.

Distribution
Paracetamol is distributed into most body tissues. Binding to the plasma proteins is minimal at therapeutic concentrations but increases with increasing doses.

Metabolism
Paracetamol is metabolised in the liver and excreted in the urine mainly as glucuronide and sulphate conjugates.

The metabolites of paracetamol include a minor hydroxylated intermediate which has hepatotoxic activity. This intermediate metabolite is detoxified by conjugation with glutathione. However, it can accumulate following paracetamol overdosage (more than 200 mg/kg or 10 g total paracetamol ingested) and, if left untreated, can cause irreversible liver damage.

Paracetamol is metabolised differently by infants and children compared to adults, the sulphate conjugate being predominant.

Excretion
Paracetamol is excreted in the urine mainly as the glucuronide and sulphate conjugates. Less than 5% is excreted as unmodified paracetamol with 85% to 90% of the administered dose eliminated in the urine within 24 hours of ingestion. The elimination half-life varies from one to three hours.

Indications

Febramol Suppositories

For fast effective temporary relief of pain and discomfort associated with immunisation, earache, cold and flu symptoms, teething and headache. Reduces fever.

Febramol Syrup

For fast effective temporary relief of pain and discomfort associated with immunisation, earache, cold and flu symptoms, teething and headache. Reduces fever.

Contraindications

Known hypersensitivity to Paracetamol.

Warnings

Renal and Hepatic impairment

Patients who have been diagnosed with liver or kidney impairment must seek medical advice before taking this medication.

Underlying liver disease increases the risk of paracetamol-related liver damage. Patients who have been diagnosed with liver or kidney impairment must seek medical advice before taking this medication. If symptoms persist, medical advice must be sought. Keep out of sight and reach of children.

Pregnancy

Category B
Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women.

Nursing Mothers

Although Paracetamol appears in very low concentration in breast milk, risk-benefit must be considered before this drug is given to nursing mothers.

Adverse Reactions

Adverse events from historical clinical trial data are both infrequent and from small patient exposure. Accordingly, events reported from extensive post-marketing experience at therapeutic/labeled dose and considered attributable are tabulated below by System Organ Class and frequency.
The following convention has been utilized for the classification of undesirable effects: very common (≥1/10), common (≥1/100, <1/10), uncommon (≥1/1,000, <1/100), rare (≥1/10,000, <1/1,000), very rare (<1/10,000), not known (cannot be estimated from available data).

Adverse event frequencies have been estimated from spontaneous reports received through post-marketing data.

Frequency	Undesirable Effect	Body System
Very rare	Thrombocytopenia	Blood and lymphatic system disorders
Very rare	Anaphylaxis Cutaneous hypersensitivity reactions including skin rashes, angioedema and Stevens Johnson syndrome	Immune system disorders
Very rare	Bronchospasm	Respiratory, thoracic and mediastinal disorders
Very rare	Hepatic dysfunction	Hepatobiliary disorders

Precautions

If a sensitivity reaction occurs, discontinue use. Paracetamol should be given with care to patients with impaired kidney or liver function.

Drug Interactions

Paracetamol/ Oral Anticoagulants

Regular administration of Paracetamol may enhance the activity of coumarin anticoagulants, when given concurrently. Occasional doses have no significant effect.

Paracetamol/ Hepatic Enzyme-inducing Agents

Concurrent administration of enzyme inducers and Paracetamol may decrease the therapeutic effect of Paracetamol, probably because of increased metabolism resulting from induction of hepatic microsomal enzyme activity.

Paracetamol/ Salicylates/ Other Non-steroidal Anti-inflammatory Drugs

Chronic high-dose administration of Paracetamol with salicylates and/or other non-steroidal anti-inflammatory drugs increases the risk of analgesic nephropathy.

Paracetamol/ Zidovudine

Paracetamol may competitively inhibit hepatic glucuronidation of zidovudine and decrease its clearance from the body. Zidovudine may also inhibit the hepatic glucuronidation of Paracetamol. Concurrent use should be avoided, because the toxicity of either or both medications may be potentiated.

Diagnostic Interference

Blood Glucose

Blood glucose determinations, when measured by the glucose oxidase/peroxidase method, may be falsely decreased; but probably not when measured by the hexokinase/glucose-6-phosphate dehydrogenase (G6PD) method.

Serum Uric Acid

Falsely increased serum uric acid values may occur when the phosphotungstate uric acid test method is used.

Urine 5-Hydroxyindoleacetic Acid (5-HIAA)
Qualitative screening tests using nitrosonaphthol may produce false-positive test results. The quantitative test is unaffected.

Pancreatic Function Test using Bentiromide
Administration of Paracetamol prior to the bentiromide test will invalidate the test results, because Paracetamol is also metabolized to an arylamine and will therefore increase the apparent quantity of para-aminobenzoic acid (PABA) recovered. It is recommended that Paracetamol be discontinued at least three days prior to administration of bentiromide.

Dosage and Administration

Syrup

Children

Age	Dosage
0-4 months	2 ml up to 4-5 times daily
4-12 months	3ml up to 4-5 times daily
1-2 years	5 ml 4-5 times daily
2-4 years	6 ml 4-5 times daily
4-6 years	10 ml 4-5 times daily
6-9 years	13 ml 4-5 times daily
9-10 years	15 ml 4-5 times daily

Adults
20 ml every 4-5 hours.
"Note: Do not exceed 4 grams of Paracetamol (166 ml) in any 24-hour period."

Suppositories

Infant 150 Suppositories
Up to 3 years one suppository up to 5 times daily

Children's 300 Suppositories
3-6 years 1 suppository 4-5 times daily
6-11 years 2 suppositories 4-5 times daily

Over Dosage

Manifestations

In massive over dosage, Paracetamol may cause hepatic toxicity. Early symptoms following a potentially hepatotoxic overdose may include nausea, vomiting, diaphoresis, and general malaise. Clinical and laboratory evidence of hepatic toxicity may not be apparent until 48-72 hours post-ingestion.

Serious toxicity or fatalities are extremely infrequent in children, possibly due to differences in the way they metabolize Paracetamol. An acute overdose of less than 150 mg/kg body weight in children has not been associated with hepatic toxicity.

Treatment

Adults and Adolescents

Regardless of the quantity of Paracetamol reported or assumed to have been ingested, N-acetylcysteine should be administered immediately, if 24 hours or less has elapsed from the time of ingestion.

An initial dose of 150 mg N-acetylcysteine/kg body weight infused I.V. in 200 ml of 5% Dextrose Injection over 15 minutes. This followed by I.V. infusion of 50 mg N-acetylcysteine/kg body weight in 500 ml of 5% Dextrose Injection over the next 4 hours, and 100 mg N-acetylcysteine/kg body weight in 1 litre of 5% Dextrose Injection over the next 16 hours (providing a total dose of 300 mg/kg body weight of N-acetylcysteine over 20 hours).

In addition to N-acetylcysteine administration, it is recommended that the stomach be emptied promptly by lavage, or by induction of emesis with syrup of ipecac.

A serum Paracetamol assay should be obtained as early as possible, but not less than 4 hours following ingestion.
Liver function tests should be performed initially, and repeated at 24-hour intervals.

Children

Induce emesis-using syrup of ipecac.
A serum Paracetamol assay should be obtained as soon as possible, but not less than 4 hours following ingestion. If the assay indicates that, more than 150 mg/kg body weight has been ingested, or if a Paracetamol assay is not available but it is estimated that such an amount has indeed been ingested, N-acetylcysteine therapy should be initiated and continued for a full course.

The dosage and administration of N-acetylcysteine in children is the same as recommended for adults and adolescents. However, the quantity of I.V. fluid used in children should be modified, taking into account both age and weight.

Presentation

Febramol 150 Suppositories

Box of 6 suppositories.

Febramol 300 Suppositories

Box of 6 suppositories.

Febramol Syrup

Bottle of 100 ml.