

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Paracetamol Adult 500mg/5ml oral suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5ml contains 500mg Paracetamol

Excipients:

Methyl parahydroxybenzoate – 6mg/5ml

Propyl parahydroxybenzoate – 1.5mg/5ml

Liquid maltitol – 2.05g/5ml

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oral suspension

An opaque pink/brown suspension

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the treatment of mild to moderate pain in patients who are unable to receive other paracetamol formulations such as lower strength liquid preparations, effervescent tablets or tablets.

4.2 Posology and method of administration

Posology

Adults and adolescents over 16 years: 500mg (5ml) or 1000mg (10ml) up to three to four times a day, as required. Maximum daily dose should not exceed 4g (40ml).

The dose should not be repeated more frequently than every four hours, and not more than four doses should be taken in any 24 hour period.

Special Populations

Renal impairment:

When a 500 mg administration is possible:

It is recommended, when giving paracetamol to patients with renal impairment, to reduce the dose and to increase the minimum interval between each administration to at least 6 hours unless directed otherwise by a physician. See Table below:

Adults:

Glomerular filtration rate	Dose
10-50 ml/min	500mg every 6 hours
<10ml/min	500mg every 8 hours

Hepatic impairment:

In patients with hepatic impairment or Gilbert's Syndrome, the dose should be reduced or the dosing interval prolonged.

The daily dose should not exceed 2g/day unless directed by a physician.

The elderly:

Experience has indicated that normal adult dosage is usually appropriate. However in frail, immobile, elderly subjects or in elderly patients with renal or hepatic impairment, a reduction in the amount or frequency of dosing may be appropriate.

The maximum daily dose should not exceed 60mg/kg/day (up to a maximum of 2g per day) in the following situations, unless directed by a physician:

- Weight less than 50kg
- Chronic alcoholism
- Dehydration
- Chronic malnutrition

Method of administration

For oral administration only

Method of administration

For oral administration only

4.3 Contraindications

Hypersensitivity to paracetamol or to any of the excipients listed in section 6.1.
Patients with severe hepatic dysfunction.

Do not use this medicine in children and adolescents under 16 years.

4.4 Special warnings and precautions for use

Paracetamol should be administered with caution under the following circumstances (see section 4.2 where relevant):

- Hepatic impairment
- Chronic alcoholism
- Renal impairment (GFR \leq 50ml/min)
- Gilbert's Syndrome (familial non-haemolytic jaundice)
- Concomitant treatment with medicinal products affecting hepatic function
- Glucose-6-phosphate dehydrogenase deficiency
- Haemolytic anaemia
- Glutathione deficiency
- Dehydration
- Chronic malnutrition
- Weight less than 50kg
- Elderly

In general, medicinal products containing paracetamol should be taken for only a few days without the advice of a physician or dentist and not at high doses.

If high fever or signs of secondary infection occur or if symptoms persist for longer than 3 days, a physician should be consulted.

Prolonged or frequent use is discouraged. Patients should be advised not to take other paracetamol containing products concurrently. Taking multiple daily doses in one administration can severely damage the liver; in such case medical assistance should be sought immediately.

Care is advised in the administration of paracetamol to patients with severe renal or severe hepatic impairment. The hazards of overdose are greater in those with non-cirrhotic alcoholic liver disease.

Do not take with any other paracetamol-containing products.

Immediate medical advice should be sought in the event of an overdose, even if you feel well, because of the risk of delayed serious or irreversible liver damage.

Patients should be advised that paracetamol may cause severe skin reactions. If a skin reaction such as skin reddening, blisters, or rash occurs, they should stop use and seek medical assistance right away.

Do not exceed the recommended dose.

Keep out of the sight and reach of children.

Excipient warnings:

This product contains the following excipients:

Parahydroxybenzoates: these may cause allergic reactions (possibly delayed).

Liquid maltitol: patients with rare hereditary problems of fructose intolerance should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interactions

The hepatotoxicity of Paracetamol, particularly after overdose, may be increased by drugs which induce liver microsomal enzymes such as barbiturates, tricyclic antidepressants and alcohol.

The speed of absorption of paracetamol may be increased by metoclopramide or domperidone, however, concurrent use need not be avoided.

Absorption is reduced by colestyramine. Therefore, the colestyramine should not be taken within one hour if maximal analgesia is required.

Chloramphenicol: Increased plasma concentration of chloramphenicol.

The anticoagulant 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.

Antivirals: Regular use of Paracetamol possibly reduces metabolism of Zidovudine (increased risk of neutropenia).

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 quantities. Available published data do not contraindicate breast feeding.

4.7 Effects on ability to drive and use machines

None

4.8 Undesirable effects

Adverse effects of paracetamol are rare but hypersensitivity including skin rash may occur. There have been reports of blood dyscrasias including thrombocytopenia and agranulocytosis, but these were not necessarily causality related to paracetamol.

Very rare cases of serious skin reactions have been reported.

Cases of acute pancreatitis have been reported. Paracetamol has been widely used and reports of adverse reactions are rare, and are generally associated with overdose.

Allergic reactions occur occasionally.

Nephrotoxic effects are uncommon and have not been reported in association with therapeutic doses, except after prolonged administration.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continuing monitoring of the benefit/ risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL – Dublin 2. Tel: +353 16764971, Fax: +353 16762517. Website: www.hpra.ie e-mail: medsafety@hpra.ie

4.9 Overdose

Paracetamol overdose can result in liver damage which may be fatal. 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).

Overdose of paracetamol can cause liver cell necrosis likely to induce complete and irreversible necrosis, resulting in hepatocellular insufficiency, metabolic acidosis and encephalopathy which may lead to coma and death. Simultaneously, increased levels of hepatic transaminases (AST, ALT), lactate dehydrogenase and bilirubin are observed together with increased prothrombin levels that may appear 12 to 48 hours after administration.

Liver damage is likely in patients who have taken more than the recommended amounts of paracetamol. It is considered that excess quantities of toxic metabolite become irreversibly bound to liver tissue.

Some patients may be at increased risk of liver damage from paracetamol toxicity:

Risk factors

If the patient

1. Patients with liver disease
2. Elderly patients
3. Young children
4. Is on long term treatment with carbamazepine, phenobarbital, phenytoin, primidone, rifampicin, St. John's Wort or other drugs that induce liver enzymes. or
5. Regularly consumes ethanol in excess of recommended amounts. or
6. Is likely to be glutathione depleted e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia.

Symptoms

Symptoms of paracetamol overdose generally appear within the first 24 hours and are pallor, nausea, vomiting, anorexia and abdominal pain or patients may be asymptomatic. 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 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 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 24 hours from ingestion should be discussed with the NPIS or a liver unit.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Analgesics and antipyretics, Anilides
ATC Code: N02 BE01

The mechanism of analgesic action has not been fully determined. Paracetamol may act predominantly by inhibiting prostaglandin synthesis in the central nervous system

(CNS) and, to a lesser extent, through a peripheral action by blocking pain impulse generation. The peripheral action may also be due to inhibition of prostaglandin synthesis or to inhibition of the synthesis or actions of other substances that sensitise pain receptors to mechanical or chemical stimulation.

Paracetamol probably produces antipyresis by acting centrally on the hypothalamic heat regulating centre to produce peripheral vaso-dilation resulting in increased blood flow through the skin, sweating and heat loss. The central action probably involves inhibition of prostaglandin synthesis in the hypothalamus.

5.2 Pharmacokinetic properties

Oral absorption is rapid and almost complete, it may be decreased if paracetamol is taken following a high carbohydrate meal.

There is no significant protein binding with doses producing plasma concentrations below 60mcg (μg)/ml, but may reach moderate levels with high or toxic doses.

Approximately 90 - 95% of a dose is metabolised in the liver, primarily by conjugation with glucuronic acid, sulphuric acid and cysteine. An intermediate metabolite, which may accumulate in overdose after primary metabolic pathways become saturated, is hepatotoxic and possibly nephrotoxic.

Half life is 1 to 4 hours; does not change with renal failure but may be prolonged in acute overdose, in some forms of hepatic disease, in the elderly, and in the neonate; may be somewhat shortened in children.

Time to peak concentration, 0.5 - 2 hours; peak plasma concentrations, 5 - 20mcg (μg)/ml (with doses up to 650mg); time to peak effect, 1 - 3 hours; duration of action, 3 - 4 hours.

Elimination is by the renal route, as metabolites, primarily conjugates, 3% of a dose may be excreted unchanged.

Peak concentrations of 10 - 15mcg (μg)/ml have been measured in breast milk, 1 - 2 hours following maternal ingestion of a single 650mg dose. Half life in breast milk is 1.35 - 3.5 hours.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Propylene glycol (E1520)
Methyl parahydroxybenzoate (E218)
Propyl parahydroxybenzoate (E216)
Liquid maltitol (E965)
Saccharin sodium
Acesulfame potassium (E950)
Sodium dihydrogen phosphate dihydrate
Disodium hydrogen phosphate dihydrate
Magnesium aluminium silicate
Masking flavour (containing propylene glycol (E1520))
Strawberry flavour (C9987) (containing propylene glycol (E1520))
Purified water

6.2 Incompatibilities

In the absence of compatibility studies this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

24 months
1 month once open

6.4 Special precautions for storage

Do not store above 25°C. Do not refrigerate or freeze. Store in the original package.

6.5 Nature and contents of container

Bottle: Amber (Type III) glass with capacity of 150ml.

Closure: HDPE, EPE wadded, tamper evident, child resistant closure

Syringe: Polypropylene body and plunger with a capacity of 5ml.

Bottle adaptor: Low Density Polyethylene.

6.6 Special precautions for disposal

Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Rosemont Pharmaceuticals Ltd
Rosemont House
Yorkdale Industrial Park
Braithwaite Street
Leeds
LS11 9XE
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA0312/020/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 5th April 2012
Date of last renewal: 15th December 2016

10 DATE OF REVISION OF THE TEXT

November 2018