

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Paracetamol 500 mg, Guaifenesin 200 mg, Phenylephrine Hydrochloride 10 mg, Powder for Oral Solution.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One sachet contains:

500mg Paracetamol

200mg Guaifenesin

10mg Phenylephrine hydrochloride

Excipients:

Sucrose 2000 mg

Aspartame 6 mg

Sodium 157 mg

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Powder for oral solution, sachet

Off-white powder

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Short term symptomatic relief of mild to moderate pain, fever, nasal congestion with an expectorant effect on chesty cough, associated with colds, chills and influenza..

4.2 Posology and method of administration

Dissolve the contents of one sachet in a standard mug of hot, but not boiling, water (approx. 250ml;). Allow to cool to a drinkable temperature.

Adults, the Elderly and children aged 12 years and over: One sachet

Repeat every four hours as required, but do not exceed four doses (sachets) in any 24 hours.

Do not give to children under 12 years, except on medical advice.

Do not give to patients with hepatic or severe renal impairment (see Section 4.3).

Seek medical advise if symptoms persist for more than 3 days.

4.3 Contraindications

Hypersensitivity to paracetamol, guaifenesin, phenylephrine hydrochloride or any of the other ingredients

Hepatic or severe renal impairment

Hypertension

Hyperthyroidism

Diabetes

Heart disease

Narrow-angle glaucoma

Porphyria

Use in patients taking tricyclic antidepressants

Use in patients who are currently taking or have taken monoamine oxidase inhibitors (MAOIs) within the last 2 weeks

Use in patients taking beta-blocking drugs

Use in patients who are currently taking other sympathomimetic drugs

Children under 12 years

4.4 Special warnings and precautions for use

Long term use of the product is not recommended.

Patients should be advised not to take with other paracetamol-containing products or other products containing the same active ingredients as this preparation. They should also be advised not to take other cough, cold or decongestant products concurrently, or alcohol. The physician or pharmacist should check that sympathomimetic-containing preparations are not simultaneously administered by several routes, i.e. orally and topically (nasal, aural and eye preparations).

This medicine should only be recommended if all symptoms (pain and/or fever, nasal congestion and chesty cough) are present.

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

Use with caution in patients receiving digitalis, beta-adrenergic blockers, methyldopa or other anti-hypertensive agents (see section 4.5)

Use with caution in patients with prostatic hypertrophy as they may be susceptible to urinary retention.

Sympathomimetic-containing products should be used with great care in patients receiving phenothiazines.

Use in patients with Raynaud's phenomenon.

Contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrose-isomaltase insufficiency should not take this medicine.

Contains sodium 157 mg per dose. To be taken into consideration by patients on a controlled sodium diet.

Contains aspartame (E951) a source of phenylalanine. May be harmful for people with phenylketonuria.

4.5 Interaction with other medicinal products and other forms of interaction

The hepato-toxicity of paracetamol may be potentiated by excessive intake of alcohol. The speed of absorption of paracetamol may be increased by metoclopramide or domperidone and absorption reduced by colestyramine.

Drugs which induce hepatic microsomal enzymes, such as alcohol, barbiturates, monoamine oxidase inhibitors and tricyclic antidepressants, may increase the hepatotoxicity of paracetamol, particularly after overdosage.

Isoniazid reduces the paracetamol clearance, with possible potentiation of its action and/or toxicity, by inhibition of its metabolism in the liver.

Probenecid causes an almost 2-fold reduction in clearance of paracetamol by inhibiting its conjugation with glucuronic acid. A reduction in the paracetamol dose should be considered if it is to be used concomitantly with probenecid.

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

Hypertensive interactions occur between sympathomimetic amines such as phenylephrine and monoamine oxidase inhibitors. Phenylephrine may adversely interact with sympathomimetic agents and may reduce the efficacy of beta-blocking drugs, methyldopa and other antihypertensive drugs (see section 4.4). Conditions where these drugs are used are contraindications for the product.

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.

Pharmacological interactions involving paracetamol with a number of other drugs have been reported. These are considered to be of unlikely clinical significance in acute use at the dosage regimen proposed.

Salicylates/aspirin may prolong the elimination $T_{1/2}$ of paracetamol.

Paracetamol may decrease the bioavailability of lamotrigine, with possible reduction of its effect, due to a possible induction of its metabolism in the liver

There is a possibility that digitalis may sensitise the myocardium to effects of sympathomimetic drugs.

Paracetamol may affect phosphotungstate uric acid tests and blood sugar tests

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 a clinically significant amount. Available published data do not contraindicate breast feeding.

There are limited data on the use of phenylephrine in pregnant women. Vasoconstriction of uterine vessels and reduced uterine blood flow associated with use of phenylephrine may result in foetal hypoxia. Until more information is available, use of phenylephrine should be avoided during pregnancy, unless considered essential by the physician.

There are no data available on whether phenylephrine is released into breast milk and no reports on the effects of phenylephrine on the nursing infant. Until more data are available, use of phenylephrine should be avoided in lactating women, unless considered essential by the physician.

The safety of guaifenesin in pregnancy and lactation has not been fully established. The product should only be used in pregnancy when considered essential by the doctor.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. When performing these activities, the possibility of adverse effects, such as dizziness and confusion should be taken into account.

4.8 Undesirable effects

The frequency of occurrence of undesirable effect is usually classified as follows:

Very common (> 1/10)

Common ($\geq 1/100$ to < 1/10)

Uncommon ($\geq 1/1,000$ to < 1/100)

Rare ($\geq 1/10,000$ to < 1/1,000)

Very rare (< 1/10,000)

Not known (incidence cannot be assessed on the basis of the available data).

Cardiac disorders: Phenylephrine may rarely be associated with tachycardia ($\geq 1/10,000$ to $\leq 1/1,000$).

Blood and lymphatic system disorders; Very rarely (1 < 1 in 10,000) blood dyscrasias e.g. thrombocytopenia, agranulocytosis, haemolytic anaemia, neutropenia, leucopenia, pancytopenia have been reported with paracetamol, but these were not necessarily causally related.

Nervous system disorders: As with other sympathomimetic amines insomnia, nervousness, tremor, anxiety, restlessness, confusion, irritability and headache may rarely occur ($\geq 1/10,000$ to $\leq 1/1,000$).

Headache and dizziness are also known to occur rarely with Guaifenesin ($\geq 1/10,000$ to $\leq 1/1,000$).

Gastrointestinal disorders: Anorexia, nausea and vomiting are common with sympathomimetics (≥ 1 in 100 to ≤ 1 in 10) to and may occur with phenylephrine.

Gastrointestinal discomfort, nausea, vomiting and diarrhoea are the most common side effects associated with Guaifenesin but these occur rarely ($\geq 1/10,000$ to $\leq 1/1,000$).

Gastro-intestinal effects of paracetamol are very rare but there have been reports of acute pancreatitis after ingestion of above normal dosage.

Renal and urinary disorders: Interstitial nephritis has been reported incidentally after prolonged use of high doses of paracetamol.

Skin and subcutaneous disorders: Hypersensitivity including skin rash and urticaria may occur rarely ($\geq 1/10,000$ to $\leq 1/1,000$) with paracetamol

Vascular disorders: High blood pressure with headache, vomiting and palpitations may occur rarely ($\geq 1/10,000$ to $\leq 1/1,000$) with phenylephrine.

Immune system disorders: There are rare reports ($\geq 1/10,000$ to $\leq 1/1,000$) of allergic or hypersensitivity reactions with both phenylephrine and paracetamol, including skin rashes, urticaria, anaphylaxis and bronchospasm.

Hepatobiliary disorders: Rarely ($> 1/10,000$ to $< 1/1,000$) Liver function test abnormal (increase in hepatic transaminases).

4.9 Overdose

PARACETAMOL

There is a risk of poisoning, particularly in elderly patients, young children, in patients with liver disease, in case of chronic alcoholism, in patients with chronic malnutrition. Overdosing may be fatal in these cases.

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 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 deplete e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia.

Symptoms

Symptoms of paracetamol overdose 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 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.

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 24h from ingestion should be discussed with the local National Poison Centre or a liver unit.

PHENYLEPHRINE HYDROCHLORIDE

Symptoms of phenylephrine overdose include irritability, headache, an increase in blood pressure and associated reflex bradycardia and arrhythmias.

Raised blood pressure should be treated with an alpha receptor antagonist such as intravenous phentolamine. Reduction of blood pressure should, by reflex mechanism, increase the heart rate but, if necessary, this can be facilitated by the administration of atropine.

GUAIFENESIN

Mild to moderate overdose may cause dizziness and gastrointestinal disturbances. Very high doses may produce excitation, confusion and respiratory depression. Urinary calculi have been reported in patients consuming large quantities of preparations containing guaifenesin.

Treatment is symptomatic, involving gastric lavage and general supportive measures.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Other cold combination preparations

ATC code: R05X

Paracetamol has both analgesic and antipyretic activity which is mediated principally through its inhibition of prostaglandin synthesis in the central nervous system.

Guaifenesin has an expectorant action. Expectorants are believed to alleviate cough discomfort by stimulating receptors in the gastric mucosa that initiate a reflex secretion of respiratory tract fluid, thereby increasing the volume and decreasing the viscosity of bronchial secretions. This facilitates removal of mucus and reduces irritation to the bronchial tissue.

Phenylephrine hydrochloride mainly acts directly on adrenergic receptors. It has predominantly α -adrenergic activity and is without significant stimulating effects on the central nervous system at usual doses. It has recognised decongestant activity and acts by vasoconstriction to reduce oedema of the nasal mucosa.

The active ingredients are not known to cause sedation.

5.2 Pharmacokinetic properties

Paracetamol is rapidly and almost completely absorbed from the gastrointestinal tract. Peak plasma concentrations are attained 10-60 minutes following oral dosing. Paracetamol is primarily metabolised in the liver via three pathways: glucuronidation, sulphation and oxidation. It is excreted in the urine, mainly as the glucuronide and sulphate conjugates. The elimination half-life ranges from 1 to 3 hours.

Guaifenesin is rapidly absorbed from the gastrointestinal tract after oral administration with maximum blood levels occurring within 15 minutes of administration. It is rapidly metabolised in the kidneys by oxidation to β -(2-methoxyphenoxy) lactic acid, which is excreted in the urine. The elimination half-life is one hour.

Phenylephrine hydrochloride is irregularly absorbed from the gastrointestinal tract and undergoes first-pass metabolism by monoamine oxidase in the gut and liver; orally administered phenylephrine thus has reduced bioavailability. It is excreted in the urine almost entirely as the sulphate conjugate. Peak plasma levels occur between 1 and 2 hours and the plasma half-life ranges from 2 to 3 hours.

5.3 Preclinical safety data

Preclinical safety data on these active ingredients in the literature have not revealed any pertinent and conclusive findings which are of relevance to the recommended dosage and use in the product and which have not already been mentioned elsewhere in this Summary.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sucrose
Citric Acid
Tartaric Acid
Sodium Cyclamate
Sodium Citrate
Aspartame (E951)
Acesulfame Potassium (E950)
Powdered Menthol
Lemon Flavour
Lemon Juice Flavour
Quinoline Yellow (E104)

6.2 Incompatibilities

None known

6.3 Shelf life

3 years

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

The sachet laminate comprises:

Ethylene/methacrylic copolymer (Surlyn) 25g/m² /aluminium foil 15 micron/Low density polyethylene 12 gm²/paper 40 gm² (outer layer).

A pack size of five and ten sachets is available.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements

7 MARKETING AUTHORISATION HOLDER

Procter & Gamble (Health & Beauty Care) Ltd
The Heights,
Brooklands,
Weybridge,
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8 MARKETING AUTHORISATION NUMBER

PA 441/43/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

October 2012