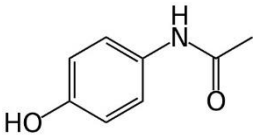
APOHEALTH COLD RELIEF TABLETS

NAME OF THE MEDICINE

Paracetamol

Chemical name: N-(4-hydroxyphenyl) acetamide.

Structural Formula:



Molecular formula: $C_8H_9NO_2$

MW: 151.2.

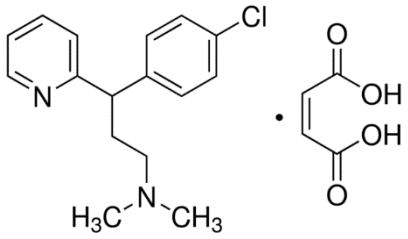
CAS Registry Number: 103-90-2

Paracetamol is a white odourless crystalline powder.

Chlorpheniramine maleate

Chemical name: 2-[p-chloro-α- (2-dimethylaminoethyl) benzyl] pyridine.

Structural Formula:



Molecular formula: $C_{16}H_{19}ClN_2,C_4H_4O_4$

MW: 390.87.

CAS Registry Number: 113-92-8

Chlorpheniramine maleate is a white odourless crystalline powder.

DESCRIPTION

Each tablet contains Paracetamol 500 mg and Chlorpheniramine maleate 2 mg. In addition each tablet also contains Cellulose – microcrystalline, Starch – Maize, Sodium starch glycollate, Povidone, Silica - colloidal anhydrous, Magnesium stearate, Opadry 04F58804 White.

PHARMACOLOGY

Pharmacological Actions

Paracetamol

Paracetamol is an analgesic and antipyretic. It relieves the elevated body temperature, headache and joint and muscle pain associated with the common cold and influenza.

Chlorpheniramine maleate

Chlorpheniramine maleate is an antihistamine. It helps to control sneezing and relieve itchy and watery eyes. The efficacy of chlorpheniramine in this product is due to its anticholinergic effect.

Pharmacokinetics

Paracetamol

Absorption: After oral administration, paracetamol is absorbed rapidly and completely from the small intestine; peak plasma levels occur 30 to 120 minutes after administration. The absorption of paracetamol is delayed by coadministration with food and anticholinergic drugs (including antihistamines).

Distribution: Paracetamol is uniformly distributed throughout most body fluids; the apparent volume of distribution is 1 to 1.2 L/kg. Paracetamol can cross the placenta and is excreted in milk.

Plasma protein binding is negligible at usual therapeutic concentrations but increases with increased concentrations.

Metabolism: Paracetamol is metabolised by the hepatic microsomal enzyme system. In adults, at therapeutic doses, paracetamol is mainly conjugated with glucuronide (45 to 55%) or sulfate (20 to 30%). A minor proportion (less than 20%) is metabolised to catechol derivatives and mercapturic acid compounds via oxidation. Paracetamol is metabolised differently by infants and children compared to adults, the sulfate conjugate being predominant.

Excretion: Paracetamol is excreted in the urine mainly as the glucuronide and sulfate conjugates. Less than 5% is excreted as unchanged 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.

Chlorpheniramine

Absorption: Chlorpheniramine is absorbed relatively slowly from the gastrointestinal tract. Peak plasma concentrations occur 2.5 to 6 hours after oral administration. It appears to undergo significant first-pass metabolism resulting in low bioavailability.

Distribution: Chlorpheniramine is approximately 70% bound to plasma proteins. Values of 2 to 43 hours have been reported as the half-life.

Metabolism: It is extensively metabolised and metabolites and unchanged drug are excreted primarily in the urine.

Excretion: Excretion is influenced by pH and urine flow rate. The duration of action has been reported to be four to six hours.

More rapid and extensive absorption, faster clearance and a shorter half-life have been reported in children.

CLINICAL TRIALS

Not available

INDICATIONS

Helps give temporary relief from the symptoms of colds and flu including headache, sneezing, body aches and pains, runny nose, watery and itching eyes, fever.

CONTRAINDICATIONS

Known hypersensitivity or intolerance to paracetamol, chlorpheniramine or any other antihistamines, or any of the excipients (**see DESCRIPTION**).

This medicine is contraindicated for use in patients with narrow angle glaucoma, stenotic peptic ulcer, pyloroduodenal obstruction and bladder neck obstruction, symptomatic prostatic hypertrophy and in patients taking monoamine oxidase inhibitors (MAOIs)

Active alcoholism may predispose patients to paracetamol hepatotoxicity.

PRECAUTIONS

This medicine should be administered with caution to patients with hepatic or renal dysfunction, epilepsy, and chronic alcohol users. Large doses of paracetamol may cause hepatic toxicity.

This medication may be dangerous when used in large amounts or for a long period.

Use in pregnancy. (Category A)

Drugs which have been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the fetus having been observed.

Use in lactation

Not recommended for use by breastfeeding mothers. Paracetamol and chlorpheniramine is excreted in breast milk.

Use in children

Not recommended in children under 12 years of age.

Use in the elderly

Dizziness, sedation and hypotension are more likely to occur in elderly patents (approximately 60 years and over).

Effect on ability to drive or operate machinery

Chlorpheniramine maleate may cause drowsiness in some patients. Such patients should be cautioned about operating vehicles or machinery or engaging in activities which require them to be fully alert. Alcohol should be avoided.

INTERACTIONS WITH OTHER MEDICINES

Paracetamol

Anticoagulant dosage may require reduction if use of the medication is prolonged.

Paracetamol absorption is increased by drugs which increase gastric emptying, e.g. metoclopramide, and decreased by drugs which decrease gastric emptying, e.g. propantheline, antidepressants with anticholinergic properties, narcotic analgesics. Paracetamol may increase chloramphenicol concentrations. The likelihood of paracetamol toxicity may be increased by the concomitant use of enzyme inducing agents such as alcohol or antiepileptic drugs.

Other possible drug interactions. Patients who have taken liver microsomal inducing drugs including barbiturates, imipramine and alcohol show diminished ability to metabolise large doses of paracetamol, the plasma half-life of which can be prolonged.
Alcohol can increase the hepatotoxicity of paracetamol.

Chlorpheniramine maleate

The sedative effect may be potentiated by concomitant use with alcohol, tricyclic antidepressants, barbiturates or other CNS depressants. Monoamine oxidase inhibitors (MAOIs) prolong and intensify the effects of antihistamines.

The action of oral anticoagulants maybe inhibited by antihistamines.

Chlorpheniramine may have an additive antimuscarinic action with other drugs with antimuscarinic properties, such as atropine and some antidepressants (both tricyclics and MAOIs) and it may mask the warning signs of damage caused by ototoxic drugs such as aminoglycoside antibiotics.
Chlorpheniramine enhances the CNS depressant effects of the hypnotic sedatives such as chloral hydrate and nitrazepam.

Alcohol enhances the CNS depressant effects of chlorpheniramine.

Serious adverse effects may occur when chlorpheniramine is given with phenytoin.

ADVERSE EFFECTS

Paracetamol

Reports of adverse reactions are rare. Although the following reactions have been reported, a causal relationship to the administration of paracetamol has neither been confirmed nor refuted. Dyspepsia, nausea, allergic and haematological reactions, as well as hepatotoxicity.

Chlorpheniramine maleate

Antihistamines such as chlorpheniramine maleate may cause disturbances of the following systems:

Central nervous system.

Sedation, dizziness, ataxia, headache. May cause excitation in children.

Cardiovascular.

Palpitations, urinary retention, blurred vision.

Gastrointestinal.

Dry mouth, nausea, vomiting, constipation or diarrhoea.

Dermatological.

Skin rashes may occur.

Haematological.

Haematalogical disturbances.

DOSAGE AND ADMINISTRATION

Adults, children > 12 years
2 tablets every 4 to 6 hours when necessary (maximum 8 tablets in 24 hours).

Not to be used in children under 12 years of age.

OVERDOSAGE

Symptoms

Paracetamol

Toxic symptoms of paracetamol include vomiting, abdominal pain, liver damage, hypotension, sweating, central stimulation with exhilaration and convulsions in children, drowsiness, gastrointestinal haemorrhage, cerebral oedema and renal tubular necrosis, respiratory depression, cyanosis and coma.

The most serious adverse effect of acute overdosage of paracetamol is a dose dependent, potentially fatal hepatic necrosis. In adults, hepatotoxicity may occur after ingestion of a single dose of paracetamol 10 to 15 g (30 tablets); a dose of 25 g (50 tablets) or more is potentially fatal. Symptoms during the first two days of acute poisoning by paracetamol do not reflect the potential seriousness of the intoxication. Major manifestations of liver failure such as jaundice, hypoglycaemia and metabolic acidosis may take at least three days to develop.

Chlorpheniramine

Overdose with chlorpheniramine is associated with antimuscarinic, extrapyramidal, gastrointestinal and CNS side effects. In infants and children CNS stimulation predominates over CNS depression, causing ataxia, excitement, tremors, psychoses, hallucinations and convulsions; hyperpyrexia may also occur. Deepening coma and cardiorespiratory collapse may follow. In adults, CNS depression is more common with drowsiness, coma and convulsions, progressing to respiratory failure or possibly cardiovascular collapse.

Treatment

Consists primarily of management of paracetamol toxicity. In cases of overdosage, methods of reducing the absorption of ingested drug are important.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

PRESENTATION AND STORAGE CONDITIONS

Presentation

Tablets (white coloured, oval shaped, biconvex, film coated, with central breakline on one side and plain on the other side.) contain Paracetamol 500 mg and Chlorpheniramine maleate 2 mg in blister pack of 24 tablets (AUST R 254172).

Storage

Store below 30°C

NAME AND ADDRESS OF THE SPONSOR

Apotex Pty Ltd
16 Giffnock Avenue
Macquarie Park NSW 2113

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POISON SCHEDULE OF THE MEDICINE

S3.

Date of first inclusion in the Australian Register of Therapeutic Goods (the ARTG):

11 August 2015