CLEAN PARAGRIP C PACKAGE INSERT

SCHEDULING STATUS:

S2

PROPRIETARY NAME AND DOSAGE FORM:

PARAGRIP C Effervescent tablets

COMPOSITION:

Each tablet contains:

Chlorphenamine maleate	2 mg
Paracetamol	500 mg
Sodium ascorbate equivalent to Vitamin C	250 mg

PHARMACOLOGICAL CLASSIFICATION:

A.5.8. Preparations for the common cold including nasal decongestants.

PHARMACOLOGICAL ACTION:

PARAGRIP C effervescent tablets have analgesic, antipyretic, antihistaminic and decongestant properties.

Pharmacokinetics:

Chlorphenamine maleate:

Chlorphenamine maleate is absorbed relatively slowly from the gastrointestinal tract, peak plasma concentration occurring about 2,5 to 6 hours after administration by mouth. Chlorphenamine appears to undergo considerable first-pass metabolism. Unchanged chlorphenamine and metabolites are excreted primarily tin the urine; excretion is dependent on urinary pH and flow rate. About 70 % of chlorphenamine in the circulation is bound to plasma proteins.

Paracetamol:

Following oral administration, paracetamol is well absorbed, with peak plasma concentrations obtained after 0,5 to 1 hour. The plasma half-life is about 2 hours. Plasma protein binding is variable. Paracetamol is metabolised in the liver primarily by conjugation with glucuronic acid (about 60 %), sulphuric acid (about 35 %) and cysteine (about 3 %). Paracetamol is renally excreted primarily as conjugated metabolites.

Sodium ascorbate:

Sodium ascorbate is readily absorbed from the gastrointestinal tract and is widely distributed in the body tissue. Plasma concentration of ascorbic acid rise as the dose ingested are increase until a plateau is reached with doses of about 90 to 150 mg daily. Excess of the body's needs is rapidly eliminated unchanged in the urine. Ascorbic acid crosses the placenta and is distributed into breast milk.

INDICATIONS:

PARAGRIP C is indicated for symptomatic relief of runny nose, sneezing, sore throat, headache and generalized aching due to colds and flu.

CONTRA-INDICATIONS:

PARAGRIP C is contra-indicated in

- Patients with hypersensitivity to any of the ingredients.
- Severe liver function impairment.
- Epilepsy.
- Children under the age of 12 years.

WARNINGS:

PARAGRIP C may lead to drowsiness and impaired concentration that may be aggravated by the simultaneous intake of alcohol or other nervous system depressants. Patients should be advised, particularly at the initiation of therapy, against taking charge of vehicles or machinery or performing potentially hazardous tasks where loss of concentration could lead to accidents.

Dosages of PARAGRIP C in excess of those recommended may cause severe liver damage. Consult a medical practitioner if pain or fever persist or gets worse at the recommended dosage, if new symptoms occur or if redness and swelling is present, as these could be signs of a more serious condition.

Do not use PARAGRIP C continuously for more than 10 days without consulting your doctor.

In the event of overdosage or suspected overdose and notwithstanding the fact that the person may be asymptomatic, the nearest doctor, hospital or poison centre must be contacted immediately.

Store in a safe place out of reach of children.

Patients suffering from hepatitis or alcoholism, or recovering from any form of liver disease, should not take excessive quantities of PARAGRIP C.

Use with caution in renal disease.

INTERACTIONS:

Paracetamol:

Hepatotoxic medicines – increase risk of hepatotoxicity.

Enzyme inducing medicines – increased risk of hepatotoxicity. Possible decrease in therapeutic effects of PARAGRIP C.

Metoclopramide – absorption of PARAGRIP C may be accelerated.

Cholestyramine – absorption of PARAGRIP C is reduced if given within one hour of cholestyramine.

Prolonged concurrent use of PARAGRIP C with salicylates increases the risk of adverse renal effects.

Chlorphenamine maleate:

Chlorphenamine maleate may enhance the sedative effect of central nervous system depressants, including alcohol, barbiturates, hypnotics, opioid analgesics, anxiolytic sedatives, and antipsychotics.

Concurrent use of MAO inhibitors may prolong and intensify the anticholinergic and CNS depressant effect of chlorphenamine maleate. Concurrent use is not recommended. Care should be observed when tricyclic antidepressants, guanethidine, reserpine, methyldopa or atropine are taken concomitantly.

Chlorphenamine maleate given with ototoxic medication may mask the symptoms of ototoxicity such as tinnitus, dizziness or vertigo.

Vitamin C:

Vitamin C should not be given for the first month after starting treatment with desferrioxamine due to increased iron toxicity.

Large doses of Vitamin C may increase serum ethinylestradiol concentrations in women taking oral contraceptives.

Concomitant use of Vitamin C and fluphenazine may result in decreased serum concentrations of fluphenazine.

PREGNANCY AND LACTATION:

The safety of this medicine during pregnancy and lactation has not been established.

DOSAGE AND DIRECTIONS FOR USE:

DO NOT EXCEED THE RECOMMENDED DOSE.

Adults and children over 12 years: One tablet every 8 hours if necessary. Dissolve one tablet in a glass of water and drink the content immediately once the whole tablet has dissolved.

SIDE EFFECTS AND SPECIAL PRECAUTIONS:

Side-effects:

Paracetamol:

Blood disorders:

Less frequent: Agranulocytosis, thrombocytopenia, leucopenia, pancytopenia, neutropenia, and anaemia.

Hepato-biliary disorders:

Less frequent: Hepatitis.

Skin and subcutaneous tissue disorders:

Less frequent: Allergic dermatitis.

Renal and urinary disorders:

Less frequent: Renal colic, renal failure, and sterile pyuria.

General disorders:

The following have been reported but the frequency is unknown: Pancreatitis, dermatitis, skin rashes and other allergic reactions. The rash is usually erythematous or urticarial but sometimes more serious and accompanied by fever and mucosal lesions.

Chlorphenamine maleate:

Immune system disorder:

Less frequent: Anaphylaxis including tightness of the chest.

Nervous system disorders:

Frequent: Drowsiness.

Less frequent: Convulsions or seizures, dizziness, increased sweating, abnormal coordination, tremor, lassitude, euphoria, nervousness, insomnia, headache.

Eye disorders:

Less frequent: Blurred vision, diplopia.

Ear and labyrinth disorders:

Less frequent: Tinnitus.

Cardiac disorders:

Less frequent: Hypotension, palpitations.

Gastrointestinal disorders:

Frequent: Dryness of mouth, nose or throat, gastrointestinal upset, loss of appetite, constipation, diarrhoea, nausea, vomiting.

Hepato-biliary disorders:

Less frequent: Cholestasis, hepatitis or other hepatic function abnormalities.

Skin and subcutaneous tissue disorders:

Less frequent: Exfoliative dermatitis.

Renal and urinary disorders:

Less frequent: Difficult or painful urination, dysuria.

General disorders:

Less frequent: Oedema, fatigue.

Vitamin C:

Blood and lymphatic system disorders:

The following has been reported but the frequency is unknown: Ascorbic acid in large doses may also result in haemolysis in patients with glucose-6-phosphate dehydrogenase deficiency.

Gastrointestinal disorders:

The following has been reported but the frequency is unknown: Large doses are reported to cause diarrhoea and other gastro-intestinal disturbances.

Renal and urinary disorders:

The following has been reported but the frequency is unknown: Large doses may result in hyperoxaluria and the formation of renal calcium oxalate calculi.

Vitamin C should be given with care to patients with hyperoxaluria and to patients with G6PD deficiency.

Tolerance may be induced with prolonged use of large doses.

Special Precautions:

See “Warnings”.

KNOWN SYMPTOMS FOR OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Prompt treatment is essential. In the event of an overdosage, consult a doctor immediately, or take the person directly to hospital. A delay in starting treatment may mean that the antidote is given too late to be effective. Evidence of liver damage is often delayed until after the time for effective treatment has lapsed.

Susceptibility to paracetamol toxicity is increased in patients who have taken repeated high doses (greater than 5 – 10 g/day) of paracetamol for several days, in chronic alcoholism, chronic liver disease, AIDS, malnutrition, and with the use of drugs that induce microsomal oxidation such as barbiturates, isoniazid, rifampicin, phenytoin and carbamazepine.

Symptoms of paracetamol overdose in the first 24 hours include pallor, nausea, vomiting, anorexia and possibly abdominal pain. Mild symptoms during the first two days of acute poisoning do not affect the potential seriousness of the overdosage.

Liver damage may become apparent 12 to 48 hours or later after ingestion, initially by elevation of the serum transaminase and lactic dehydrogenase activity, increase serum bilirubin concentration and prolongation of the prothrombin time. Liver damage may lead to encephalopathy, coma and death.

Acute renal failure with acute tubular necrosis may develop even in the absence of severe liver damage. Abnormalities of glucose metabolism and metabolic acidosis may occur. Cardiac arrhythmias have been reported.

Treatment of paracetamol overdosage:

Although evidence is limited it is recommended that any adult person who has ingested 5 – 10 grams or more of paracetamol (or child who has had more than 140 mg/kg) within the preceding four hours, should have stomach emptied by lavage (emesis may be adequate for children) and a single dose of 50 g activated charcoal given via the lavage tube. Ingestion of amounts of paracetamol smaller than this may require treatment in patients susceptible to paracetamol poisoning (see above). In patients whoa re stuperose or comatose endotracheal intubations should precede gastric lavage in order to avoid aspiration.

N-acetylcysteine should be administered to all cases of suspected overdose as soon as possible preferably within eight hours of overdose, although treatment up to 36 hours after ingestion may still be of benefit, especially if more than 150 mg/kg of paracetamol was taken. An intitial dose of 150 mg/kg N-acetylcysteine in 200 ml dextrose injection given intravenously over 15 minutes, followed by infusion of 50 mg/kg in 500 ml dextrose injection over the nest fours hours, and then 100 mg/kgy in 1000 ml dextrose injection over the next sixteen hours.

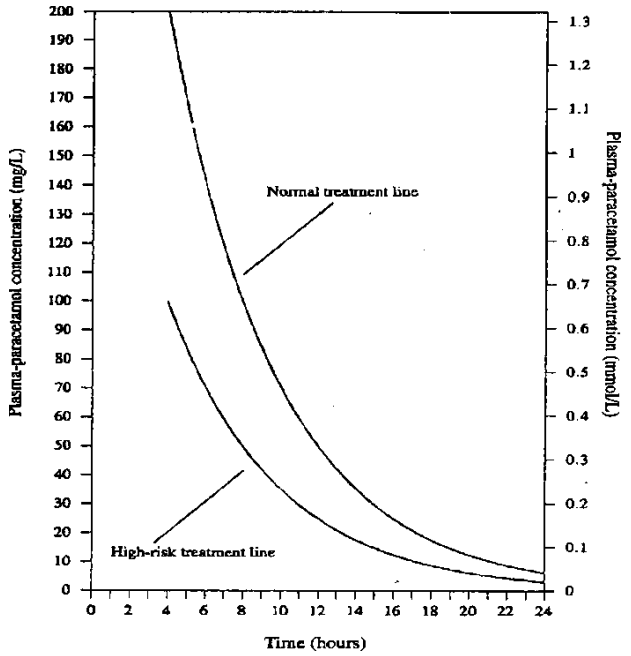
The volume of the intravenous fluid should be modified for children.

Although the oral formulation is not the treatment of choice, 140 mg/kg dissolved in water may be administered initially, followed by 70 mg/kg every four hours for seventeen doses.

A plasma paracetamol level should be determined four hours after ingestion in all cases of suspected overdose. Levels done before four hours, unless high, may be misleading. Patients at risk of liver damage and hence requiring continued treatment of N-acetylcysteine,

can be identified according to their plasma paracetamol level. The plasma paracetamol level can be plotted against time since ingestion.

A linear plot of plasma-paracetamol concentration against hours after ingestion:



1. The time coordinates refer to time after ingestion.
2. Plasma-paracetamol concentrations drawn before 4 hours may not represent peak concentrations.
3. The graph should be used only in relation to a single acute ingestion.
4. Patients whose plasma-paracetamol concentrations are above the normal treatment line should be treated.
5. Patients on enzyme-inducing drugs or with malnutrition or a history of alcohol abuse should be treated if their plasma-paracetamol concentrations are above the high-risk treatment line.

6. The value of such charts is uncertain if the patient is first seen 15 hours or more after ingestion, or has taken modified release preparations of paracetamol.

Those, whose plasma paracetamol levels are above the “normal treatment line”, should continue N-acetylcysteine treatment with 100 mg/kg IV over sixteen hours repeatedly until recovery. Patients with increase susceptibility to liver damage as identified above, should continue treatment if concentrations are above the “high risk treatment line”. Prothrombin index correlates best with survival.

Monitor all patients with significant ingestions for at least six hours.

Overdosage with PARAGRIP C may result in anticholinergic effects (unsteadiness, severe drowsiness, severe dryness of throat, nose and mouth, redness of face and shortness of breath). Convulsions, tachycardia and cardiac arrhythmias may occur.

Overdosage may be fatal, especially in infants and children in whom the main symptoms are central nervous system stimulation and antimuscarinic effects. Deepening coma, cardiorespiratory collapse and death may occur within 18 hours. In adults, the usual symptoms are of central nervous system depression with drowsiness, coma and convulsions.

Hypotension may also occur. Elderly patients are more susceptible to the central nervous system depressant and hypotensive effects even at therapeutic doses.

Treatment is symptomatic and supportive.

IDENTIFICATION:

PARAGRIP C is a white or almost white, round, flat tablet. It produces a slightly opalescent, colourless solution with a citrus flavour once dissolved in a glass of water.

PRESENTATION:

PARAGRIP C is available in white polypropylene tubes closed with a low-density polyethylene cap. Each tube contains 10, 12 or 20 tablets.

STORAGE INSTRUCTIONS:

Store at or below 25 °C in a dry place. Keep the tube tightly closed.

KEEP OUT OF REACH OF CHILDREN

REGISTRATION NUMBER:

A39/5.8/0450

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