CHESTON Expectorant/DT (Bromhexine hydrochloride + Guaiphenesin + Chlorpheniramine)

Composition

CHESTON EXPECTORANT
Each 5 ml contains:
Bromhexine Hydrochloride BP.....4 mg
Guaiphenesin IP.....50 mg
Chlorpheniramine Maleate IP.....2 mg

CHESTON DT
Each dispersible tablet contains:
Bromhexine Hydrochloride BP.....4 mg
Guaiphenesin IP.....50 mg
Chlorpheniramine Maleate IP.....2 mg

Pharmacology

Pharmacodynamics

Bromhexine Hydrochloride
Bromhexine is an oral mucolytic agent with a low level of associated toxicity. Bromhexine acts on the mucus at the formative stages in the glands, within the mucus-secreting cells. Bromhexine disrupts the structure of acid mucopolysaccharide fibres in mucoid sputum and produces less viscous mucus, which is easier to expectorate.

Guaiphenesin
Guaiphenesin is thought to exert its pharmacological action by stimulating receptors in the gastric mucosa. This increases the output from the secretory glands of the gastrointestinal system and the reflex increases the flow of fluids from glands lining the respiratory tract. The result is an increase in volume and decrease in viscosity of bronchial secretions. Other actions may include stimulating vagal nerve endings in bronchial secretory glands and stimulating certain centres in the brain, which in turn enhance respiratory fluid flow. Guaiphenesin produces its expectorant action within 24 hours.

Chlorpheniramine Maleate
Chlorpheniramine antagonises competitively the effects of histamine on H1-receptors and also has weak antimuscarinic and moderate antiserotonin and local anaesthetic actions. It penetrates the brain and causes stimulation or sedation in animals.

Pharmacokinetics

Bromhexine Hydrochloride

Bromhexine hydrochloride is rapidly absorbed from the gastrointestinal tract and undergoes extensive first-pass metabolism in the liver. Its oral bioavailability is stated to be only about 20%. It is widely distributed to body tissues and is highly bound to plasma proteins. About 85-90% of a dose is excreted in the urine mainly as metabolites. It has a terminal elimination half-life of up to about 12 hours. Bromhexine crosses the blood-brain barrier and small amounts cross the placenta.

Guaiphenesin
Guaiphenesin is well absorbed from the gastro-intestinal tract following oral administration, although limited information regarding its pharmacokinetics is available. After the administration of 600 mg guaiphenesin to healthy adult volunteers, the C_{max} was approximately 1.4 g/ml, with the t_{max} occurring approximately 15 minutes after drug administration. No information is available on the distribution of guaiphenesin in humans. Guaiphenesin appears to undergo both oxidation and demethylation. Following an oral dose of 600 mg guaiphenesin to 3 healthy male volunteers, the t- was approximately 1 hour and the drug was not detectable in the blood after approximately 8 hours.

Pharmacokinetics in Renal/Hepatic Impairment

There have been no specific studies of guaiphenesin in subjects with renal or hepatic impairment. Caution, is therefore, recommended when administering this product to subjects with severe renal or hepatic impairment.

Pharmacokinetics in the Elderly

Not applicable.

Chlorpheniramine Maleate
Chlorpheniramine maleate is almost completely absorbed after administration by mouth, peak plasma concentrations occurring at about 2.5 to 6 hours. The drug is widely distributed including passage into the CNS, with a volume of distribution of between 1 and 10 L/KG. About 70% of chlorpheniramine in the circulation is protein-bound. Chlorpheniramine undergoes some first pass metabolism and enterohepatic recycling. Chlorpheniramine is extensively metabolised, principally to inactive desmethylated metabolites which are excreted primarily in the urine, together with about 35% unchanged drug. Only trace amounts are excreted in the faeces. The mean elimination half-life has been reported to be about 30 hours, with mean values ranging from 2 to 43 hours.

Indications

CHESTON EXPECTORANT/DT is indicated for the symptomatic relief of productive cough.

Dosage and Administration

Children (aged 2-6 years)

2.5 ml or half tablet thrice daily

Children (aged 6-12 years)

5 ml or 1 tablet thrice daily

Children (aged >12 years) and adults

10 ml or 2 tablets thrice daily

Contraindications

It is contraindicated for use in patients with known hypersensitivity to any of its ingredients or in patients with severe hypertension, severe coronary artery disease, and patients on monoamine oxidase (MAO) inhibitor therapy.

Warnings and Precautions

General

Since mucolytics may disrupt the gastric mucosal barrier, bromhexine should be used with caution in patients with a history of gastric ulceration. Clearance of bromhexine or its metabolites may be reduced in patients with severe hepatic or renal impairment.

Sympathomimetic amines should be used judiciously and sparingly in patients with hypertension, diabetes mellitus, ischaemic heart disease, increased intraocular pressure, hyperthyroidism, and prostatic hypertrophy. Sympathomimetics may produce CNS stimulation with convulsions or cardiovascular collapse with accompanying hypotension.

Do not exceed the recommended dosage.

This medicine should be given with caution to patients with epilepsy, severe cardiovascular disorders, liver disorders, glaucoma, urinary retention, prostatic enlargement, pyloroduodenal obstruction, asthma, bronchitis, bronchiectasis, thyrotoxicosis and severe hypertension.

Special care should be taken when using chlorpheniramine maleate in children and the elderly as they are more prone to developing neurological anticholinergic effects.

Warning: May cause drowsiness. If affected do not drive or operate machinery. Avoid alcoholic drink.

If symptoms do not go away within 5 days talk to your pharmacist or doctor.

Keep all medicines out of the reach of children.

Although most antihistamines should be avoided by patients with porphyria, chlorpheniramine maleate has been used and is thought to be safe.

Drug Interactions

There are no known significant interactions with other medicines.

Pregnancy

Bromhexine has been taken by a large number of pregnant women and women of child bearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the foetus having been observed.

There are no adequate controlled studies of chlorpheniramine in pregnant women and this medicine should therefore not be used during pregnancy.

Drugs should be given only if the potential benefit justifies the potential risk to the foetus.

Lactation

It is not known whether bromhexine is excreted in breast milk or whether it has a harmful effect on the breastfeeding infant.

Chlorpheniramine may be secreted in breast milk and its use is not recommended in nursing mothers because of the risk of adverse effects, such as unusual excitement or irritability in infants. Chlorpheniramine may also inhibit lactation.

Therefore it is not recommended for breastfeeding mothers unless the potential benefits to the patient are weighed against the possible risk to the infant.

Undesirable Effects

Bromhexine Hydrochloride

Gastrointestinal side effects may occur occasionally with bromhexine and a transient rise in serum aminotransferase values has been reported. Other reported adverse effects include headache, vertigo (dizziness), sweating and allergic reactions.

Guaiphenesin

The following side effects may be associated with the use of Guaiphenesin:
Gastrointestinal Disorders: Nausea, vomiting
Immune System Disorders: Hypersensitivity reactions

Chlorpheniramine Maleate

The product may cause drowsiness, which may progress to deep sleep, headache, dizziness, psychomotor impairment, inability to concentrate, lassitude, irritability and antimuscarinic effects such as urinary retention, dry mouth and blurred vision. Gastrointestinal disturbances may occur including abdominal pain, dyspepsia and anorexia. Paradoxical CNS stimulation may occur especially in children or after high doses. Skin rashes including exfoliative dermatitis and photosensitivity reactions and hypersensitivity reactions including urticaria may occur. Other side effects include convulsions, sweating, myalgia, paraesthesia, tinnitus, palpitations, tachycardia, arrhythmias, chest pain, haemolytic anaemia and other blood dyscrasias, extrapyramidal effects, tremor, liver dysfunction, including hepatitis and jaundice, sleep disturbances, including nightmares, depression, hypotension, hair loss, thickening of bronchial secretions and confusional psychosis in the elderly.

Glycerol may cause headache, stomach upset and diarrhoea.

Overdosage

Bromhexine Hydrochloride

Overdose. Symptoms: nausea, vomiting, diarrhoea, dyspepsia. Treatment: artificial vomiting, gastric lavage (in the first 1-2 hours after admission).

Guaiphenesin

Symptoms and Signs
The effects of acute toxicity from guaiphenesin may include gastrointestinal discomfort, nausea and drowsiness.

Treatment
Treatment should be symptomatic and supportive.

Chlorpheniramine Maleate

Overdosage with chlorpheniramine is associated with antimuscarinic, extrapyramidal, gastrointestinal and CNS effects. In infants and children, CNS stimulation predominates over CNS depression, causing ataxia, excitement, tremors, psychosis, hallucinations and convulsions. Hyperpyrexia may also occur. Other symptoms of overdosage in children include dilated pupils, dry mouth, facial flushing. Deepening coma and cardiorespiratory collapse may follow, and even death. In adults CNS depression is more common with drowsiness, coma and convulsions, progressing to respiratory failure or possibly cardiovascular collapse including arrhythmias.

In severe overdosage the stomach should be emptied. Activated charcoal has been given as have saline laxatives. Convulsions may be controlled with diazepam or phenytoin, although it has been suggested that CNS depressants should be avoided. Other treatment is supportive and symptomatic and may include artificial respiration, external cooling for hyperpyrexia and intravenous fluids. Vasopressors such as noradrenaline or phenylephrine may be used to counteract hypotension. Forced diuresis, peritoneal dialysis or haemodialysis appear to be of limited benefit.

Packaging Information

CHESTON Expectorant: Bottles of 60 ml and 100 ml
CHESTON DT: Strip of 10 tablets

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