1.3.1.1 PROFESSIONAL INFORMATION

SCHEDULING STATUS: S2

PROPRIETARY NAME AND DOSAGE FORM:

DILINCT® (SYRUP)

COMPOSITION:

Each 15 ml contains:

Hydroxyethyltheophylline (Etofylline)	105,5 mg
Diphenhydramine hydrochloride	42,2 mg
Ammonium chloride	410,5 mg
Preservative: Nipastat	0,02 % *m/v*
Ethanol	0,482 % *v/v*
Contains sugar:	
Sucrose	9,00 g
Contains Sweetener:	
Saccharin Sodium	0,000978 g

Excipients: Polysorbate 20, sodium citrate hydrous, citric acid anhydrous, colour caramel, levomenthol, apri-passion flavour, sorbitol, calcium cyclamate, purified water.

PHARMACOLOGICAL CLASSIFICATION:

A 10.1 Antitussives and expectorants

PHARMACOLOGICAL ACTION:

Pharmacodynamic properties

Diphenhydramine HCl is an antihistamine. It has sedative, anticholinergic, and mild spasmolytic properties. Ammonium chloride is used as an expectorant.

Hydroxyethyltheophylline, is a derivative of theophylline and relaxes bronchial spasm.

Pharmacokinetics

Hydroxyethyltheophylline (Etofylline): is well absorbed orally, the rate and not the extent is decreased by food. Theophylline is distributed in all tissues, crosses the placentas and is secreted in milk. It is 40 - 60% plasma protein bound. It is extensively metabolized in the liver by demethylation and oxidation. Only 10 % is excreted as unchanged drug, rest are excreted as changed metabolites in the urine. Steady plasma levels are obtained 1 –3 days after initiation of therapy after which half-life is 6 –8 hours. In neonates approximately 50 % is excreted unchanged in urine.

Diphenhydramine hydrochloride: Diphenhydramine hydrochloride is well absorbed from the gastrointestinal tract, although high first-pass metabolism appears to affect systemic availability. Peak plasma concentrations occur about 1 to 4 hours after oral doses. Diphenhydramine is widely distributed throughout the body including the CNS. It crosses the placenta and has been detected in breast milk. Diphenhydramine is highly bound to plasma proteins. Metabolism is extensive. Diphenhydramine is excreted mainly in the urine as metabolites; little is excreted as unchanged drug. The elimination half-life has been reported to range from 2.4 to 9.3 hours.

Ammonium Chloride is absorbed from the gastrointestinal tract. The ammonium ion is converted into urea in the liver, the anion thus liberated into the blood and extracellular fluid causes a metabolic acidosis and decreases the pH of the urine; this is followed by transient diuresis.

INDICATIONS:

For the relief of coughing and to facilitate bronchodilation and expectoration.

CONTRAINDICATIONS:

The antihistamines are contraindicated in epileptics, since in large doses they may precipitate fits.
Do not use in children under 2 years of age.
Ammonium chloride: Should not be given to patients with impaired renal or hepatic functions, advanced arteriosclerosis or dehydration.

WARNINGS AND SPECIAL PRECAUTIONS

This medicine may lead to drowsiness and impaired concentration that may be aggravated by the simultaneous intake of alcohol or other central nervous system depressants.

Caution is needed in conditions such as closed-angle glaucoma, urinary retention, prostatic hyperplasia, pyloroduodenal obstruction.

Contains sucrose which may have an effect on the glycaemic control of patients with diabetes mellitus.

Contains sucrose. Patients with rare hereditary conditions such as fructose intolerance, glucose-galactose mal-absorption or sucrase-isomaltase insufficiency should not take DILINCT.

Patients with the rare hereditary condition of sorbitol intolerance should not take DILINCT.

INTERACTIONS

Hydroxyethyltheophylline (Etofylline): Theophylline clearance may be reduced by interaction with other medication including allopurinol, antiarrhythmics, cimetidine, disulfiram, fluvoxamine, macrolide antibacterials and quinolones, oral contraceptives, tiabendazole and viloxazine. The dose of the theophylline may need to be reduced. Phenytoin and other antiepileptics, ritonavir, rifampicin and sulfinpyrazone may increase theophylline clearance and the dose may need to be increased. The use of theophylline with beta blockers must be avoided. The toxic effects of theophylline, aminophylline and other xanthines are additive. Use with other xanthine medications should therefore be avoided.

Diphenhydramine inhibits the cytochrome P450 isoenzyme CYP2D6 that is partly responsible for the metabolism of some beta blockers including metoprolol and the antidepressant venlafaxine.

Sedating antihistamines, such as diphenhydramine, may enhance the sedative effects of CNS depressants including alcohol, barbiturates, hypnotics, opioid analgesics, anxiolytic sedatives and anxiolytics.

Sedating antihistamines, such as diphenhydramine, have an additive antimuscarinic action with other antimuscarinic drugs, such as atropine and some antidepressants (both tricyclics and MAOIs).

HUMAN REPRODUCTION

Safety in pregnancy and lactation has not been established.

DOSAGE AND DIRECTIONS FOR USE:

1 medicine measure = 5 ml.

Adults: 3 medicine measures three to four times daily.

Children: 2 to 6 years: ½ medicine measure, three to four times daily.

6 to 12 years: 1 medicine measure, three to four times daily.

Not recommended for children under 2 years of age.

SIDE EFFECTS

Hydroxyethyltheophylline (Etofylline):

May give rise to the following side effects:

System Organ Class	**Adverse Effect**	**Frequency**
Psychiatric disorders	Irritability, anxiety, restlessness and confusion.	Unknown
Nervous system disorders	CNS stimulation, insomnia, tremors. Overdosage of theophylline may lead to convulsions.	Frequent
Cardiac disorders	Palpitations.	Unknown
Gastrointestinal disorders	Nausea, vomiting, diarrhoea, abdominal pain.	Unknown
General disorders and administration site conditions	Headache.	Unknown

Diphenhydramine hydrochloride: May give rise to the following side effects:

System Organ Class	**Adverse Effect**	**Frequency**
Immune system disorders	Hypersensitivity reactions (cross-sensitivity to related drugs may occur)	Unknown
Psychiatric disorders	Sedation, drowsiness, lassitude.	Frequent
Nervous system disorders	Dizziness, incoordination; CNS stimulation (especially in children) with insomnia, nervousness, euphoria, irritability, tremors, nightmares, hallucinations and convulsions.	Unknown
Cardiac disorders	Transient bradycardia followed by tachycardia with palpitations and arrhythmias.	Unknown
Eye Disorders	Blurred vision	Unknown

Respiratory, thoracic and mediastinal disorders	Thickened respiratory tract secretions, tightness of the chest.	Unknown
Gastrointestinal disorders	Reduction in tome and motility of the gastrointestinal tract resulting in, constipation and increased gastric reflux. Nausea, vomiting, diarrhoea, gastric pain.	Unknown
General disorders and administration site conditions	Urinary difficulty and retention.	Unknown

Ammonium chloride: Is irritant to the gastric mucosa and may produce nausea and vomiting particularly in large doses. Ammonium chloride can also produce a transient diuresis and mild acidosis.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

Overdosing usually causes nausea and vomiting and possibly cardiac arrest and collapse. Respiratory and cardiac depression and collapse must be prevented and treated with artificial respiration, analeptics and oxygen - maintain blood pressure and control convulsions. Treatment is symptomatic and supportive.

IDENTIFICATION:

A brown, clear, viscous syrup with a fruity odour and an “apri-passion” taste, it should be clear and free from visible matter

PRESENTATION:

100 ml and 200 ml in amber glass bottles.

STORAGE INSTRUCTIONS:

Store in a cool place at or below 30 °C.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:

G1115 (Act 101/1965)

NAME AND BUSINESS ADDRESS OF APPLICANT:

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