National Agency for Food & Drug Administration & Control (NAFDAC)

Registration & Regulatory Affairs (R & R) Directorate

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC) TEMPLATE

1. NAME OF THE MEDICINAL PRODUCT
Cofex Syrup

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5ml contains:
Chlorpheniramine Maleate ……2mg
Ammonium Chloride ……50mg
Ipecacuanha Tincture ……0.1ml
Anise Water conc……0.1ml
Sodium Citrate ……50mg
Citric Acid ……10mg
Menthol……1.0mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Cofex Syrup is presented as a red coloured clear syrup.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
Cofex is useful in the symptomatic relief and control of coughs. It has antihistamine, expectorant and demulcent actions and helps promote the expulsion of secretions from the respiratory tract thereby reducing bronchial and nasal congestion.

4.2 Posology and method of administration
Adults and children 12 years and above
10ml three times daily.

Children
3 months – 1 year: 2.5ml three times daily.
2 – 5 years: 5ml three times daily.
6-12 years: 5 – 10ml three times daily.

Method of administration
For oral administration.

4.3 Contraindications
This product is contraindicated in individuals with known hypersensitivity to any of the components of the preparation listed in section 6.1.

The product is contra-indicated in patients who are hypersensitive to any of the components of the preparation and in neonates and premature infants owing to their increased susceptibility to the antimuscarinic effect of Chlorpheniramine anti-histamine. It is also contra-indicated in patients with hepatic or renal impairment and in acute attacks of asthma.

4.4 Special warnings and precautions for use
May cause drowsiness. If affected, do not drive or operate machinery.
Avoid alcoholic drinks.
Avoid taking on an empty stomach. Cofex Lozenges when taken with food is well tolerated.
Large doses may produce an irritant effect on the gastric mucosa causing nausea, vomiting and diarrhoea.

4.5 Interaction with other medicinal products and other forms of interaction
The action of ipecacuanha may be delayed or diminished if it is given with or after charcoal. Antiemetics may also diminish its effects.

Chlorpheniramine may enhance the sedating effects of CNS depressants including alcohol, barbiturates, hypnotics, opoid analgesics, anxiolytic sedatives and psychotics. It is incompatible with calcium chloride, kanamycin sulphate, noradrenaline tartrate and meglumine adiopone.
It has additive antimuscarinic action with other antimuscarinic drugs like atropine, tricyclic antidepressants,

and MAOIs.
It has been suggested that sedating antihistamins could mask the warning signs of damage caused by ototoxic drugs such as aminoglycoside antibiotics.
Chlorpheniramine may suppress cutaneous histamine response to allergen extracts. Its therapy should be stopped several days before skin testing.

Citrate salts like Sodium citrate can enhance the absorption of Aluminium from the GIT.

4.6 Fertility, pregnancy and lactation
The product should be used with caution in pregnancy and lactation.

4.7 Effects on ability to drive and use machines
May cause drowsiness. If affected, do not drive or operate machinery.

4.8 Undesirable effects
Side effects are rare and usually mild and may be reduced by giving the drug with meals. Large doses have an irritant effect on the gastrointestinal tract and are reported to cause gastrointestinal disturbances like nausea, vomiting and diarrhoea.

Large doses of Ammonium Chloride may cause profound acidosis and hypokalemia. Hepatic encephalopathy due to the inability of the liver to convert increased load of ammonium ions to urea has also been reported from excessive doses.

The absorption of emetine which is most likely if vomiting does not occur after overdose of ipecacuanha, may give rise to adverse effects on the heart, such as conduction abnormalities or myocardial infarction. These combined with dehydration due to vomiting may cause vasomotor collapse followed by death.

4.9 Overdose
In large doses, Ammonium Chloride may produce nausea and vomiting. Profound acidosis and hypokalemia may also occur.
Persistent bloody vomiting and bloody diarrhoea and mucosal erosions of the entire GIT has been reported following large doses of ipecacuanha.

Management:
After acute overdosage, activated charcoal should be given to delay absorption followed if necessary by gastric lavage. Further treatment should be symptomatic and along supportive lines

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties

Chlorpheniramine:
Chlorpheniramine is an akylamine derivative with the actions and uses of the antihistamines. It has significant sedative properties. It also has anti-muscarinic properties.
Chlorpheniramine diminishes or abolishes the main actions of histamine in the body by competitive, reversible blockade of histamine receptor sites on the tissues. It does not inactivate or prevent the release or synthesis of histamine.
Chlorpheniramine is often used in combination preparations for the treatment of coughs and colds. The mechanism of its antitussive action may involve reduction in cholinergic nerve transmission or may simply result from its sedative effects.

Ammonium Chloride:
Ammonium Chloride is an ammonium salt, which possesses expectorant properties useful in the treatment of productive cough.
Expectorants are considered to increase the volume of secretions in the respiratory tract thereby facilitating their removal by ciliary action and coughing. They are believed to achieve this by a reflex irritant effect on the gastric mucosa.

Ipecacuanha:
Ipecacuanha Extract is prepared from the dried underground organs of *Cephalis ipecacuanha* or of *C.*

acuminata. It has been used as an expectorant in productive cough in dosed of up to about 1.4mg of total alkaloids. It is used in larger doses as an emetic.

Concentrated Anise Water:
Concentrated Anise water is prepared from Aniseed oil which is a carminative and is mildly expectorant. It is a common ingredient of cough preparations. It is also a flavour.

Sodium Citrate:
Sodium citrate is a bicarbonate-producing salt and has an alkaline nature. It has expectorant action and is used as a common ingredient in cough mixtures.

Citric Acid:
Citric acid is mildly expectorant and has been used in preparations for the treatment of coughs, gastrointestinal disturbances and metabolic acidosis.

Menthol:
Menthol is either extracted from peppermint oil (which contains 30-50% concentration of menthol) or prepared synthetically. It is used chiefly to relieve symptoms of bronchitis, sinusitis and similar conditions. In small doses by mouth, menthol has a carminative action. It exerts a muscle relaxant action on the gut.

5.2 Pharmacokinetic properties

Chorpheniramine Maleate:
Chlorpheniramine is absorbed slowly from the GIT, peak plasma concentration occurring about 2.5 to 6 hours after administration. Chlorpheniramine appears to undergo considerable first-pass metabolism. About 70% of chlorpheniramine in the circulation is bound to plasma proteins.
There is wide inter-individual variation in the pharmacokinetics of chlorpheniramine; values ranging from 2 to 43 hours have been reported for the half-life. Chlorpheniramine is widely distributed in the body and enters the CNS.
Chlorpheniramine is extensively metabolised. Metabolites include desmethyl- and didesmethyl-chlorpheniramine. Unchanged drug and metabolites are excreted primarily in the urine; excretion is dependent on urinary PH and flow rate. Only trace amounts have been found in the faeces.
More rapid and extensive absorption, faster clearance and a shorter half-life have been reported in children.

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

Sodium Citrate:
Sodium Citrate is metabolised after absorption to bicarbonate. In the absence of a deficit of bicarbonate in the plasma, bicarbonate ions are excreted in the urine, which is rendered alkaline, and there is an accompanying diuresis.

Menthol:
After absorption, menthol is excreted in the urine and bile as a glucuronide.

5.3 Preclinical safety data
None.

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Sucrose
Aspartame
Sodium Benzoate.
Sorbitol Solution 70%
Glycerol
Sodium Carboxymethyl Cellulose

Sweet Cherry Flavour
FD & C Yellow No. 40 (Allura Red)
Menthol Crystals
Deionised Water

6.2 Incompatibilities
None known.

6.3 Shelf life
3 years.

6.4 Special precautions for storage
Store below 30°C. Protect from light.

6.5 Nature and contents of container
Pet bottles containing 10oml product placed in a printed carton.

6.6 Special precautions for disposal and other handling
None.

7. APPLICANT/MANUFACTURER
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