COREX-D Cough Syrup

1. NAME OF THE MEDICINAL PRODUCT

COREX-D

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

COREX-D Cough Syrup is available in bottle of 60 ml and 120 ml.

Each 5ml contains:

- Dextromethorphan HBr 10 mg
- Chlorpheniramine 4 mg
- Ephedrine HCl 5 mg
- Sodium Citrate 150 mg

Description

COREX-D Syrup is an antitussive agent that works by blocking the action of histamine in the body.[1]

3. PHARMACEUTICAL FORM

Syrup

4. CLINICAL PARTICULARS

4.1. THERAPEUTIC INDICATIONS

It is used for relieving symptoms of sinus pressure, sinus congestion, runny nose, itching of the throat and nose, watery eyes, and sneezing due to upper respiratory infections, hay fever and allergies.[1]

4.2. POSOLOGY AND METHOD OF ADMINISTRATION

Dosage:

Adults: 1 to 2 teaspoon 3 times a day.
Children: 6 to 12 years, 1/2 to 1 teaspoon 3 times a day.

Children: 6 to 2 years: as prescribed by the physician according to age.

Not recommended in children below 2 years.

4.3. CONTRAINDICATIONS

Do not use this medicine if allergic to it or taking or have taken sodium oxybate, furazolidone or a monoamine oxidase inhibitor within the last 14 days.

4.4. SPECIAL WARNINGS AND PRECAUTIONS FOR USE[10]

Precautions - Before Taking COREX-D:[1]

Do not use this medicine if allergic to it or taking or have taken sodium oxybate, furazolidone or a monoamine oxidase inhibitor within the last 14 days.

Before using this drug, inform doctor if having anyone of this condition; breathing problems, glaucoma, heart problems, liver disease, high blood pressure, seizures, overactive thyroid, stomach problems or urination problems.

This medicine is usually recommended only for a short time until your symptoms are cleared. Do not take it for longer than 7 days in a row.

Dextromethorphan HBr:

Special Precautions to Be Taken:

- Avoid simultaneous use with nonselective monoamine oxidase inhibitors (MAO inhibitors) – serotonin syndrome.
- May cause hallucinations, confusion, agitation, overactive reflexes, shivering, twitching of muscles and rapid heart rate
- Not for use in children under 4 years old and use caution when using in children younger than 6 years old.
- Use caution in patients who are sedated, debilitated or confined to a supine position.[8]
- As per FDA recommendation, Dextromethorphan is safe to use during pregnancy. (Category – C)[7]

Tolerance, Dependence & Withdrawal:

The level and likelihood of experiencing tolerance and dependence will ultimately depend on the dose and frequency of use. When it is abused regularly, Dextromethorphan can actually cause some of the symptoms (i.e., insomnia and dysphoria) that it is designed to cure. In addition, high-dose chronic use of Dextromethorphan can lead to the development of toxic psychosis - a mental condition characterized by a loss of contact with reality along with a confused state - as well as other physiological and behavioral problems.[5]

Chlorpheniramine:

Dosage in Hepatic Insufficiency:[7]

Caution is warranted if chlorpheniramine is considered for use in patients with compromised hepatic function. Although studies related to the clearance of chlorpheniramine in humans are limited, apparently the drug is substantially cleared via hepatic metabolism. No sufficient data available to support utilization of chlorpheniramine in patients with liver impairment.

Use in Pediatrics:[7]

Reports of infant deaths have been associated with Over-The-Counter (OTC) cough and cold medications, and chlorpheniramine is commonly used as an antihistamine, alone or in combination with a cough suppressant, a decongestant, and/or an expectorant in the OTC cough and cold products.

In January 2008, the US Food and Drug Administration issued a public health advisory recommending that cough and cold products not be used in children younger than 2 years due to the risk of serious and life-threatening effects.

4.5. INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

Information not available

4.6. FERTILITY, PREGNANCY AND LACTATION

Information not available

4.7. EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Dizziness & Drowsiness Associated with Active Ingredients in Cough Syrup:

Cough suppressants like Dextromethorphan along with anti-histamine can cause drowsiness.

Opioid analgesics (Dextromethorphan) are more likely to impair driving ability in opioid-naive patients. The miotic effects of opioids, which do not wear off with continued treatment, can cause decreased night vision. Patients starting opioid therapy should be advised to avoid driving for at least 4–5 days.

Driving ability is less likely to be impaired in patients stabilized on long-term opioid therapy, although they should also avoid driving for a few days after a dose increase.

Chlorpheniramine, as a sedative anti-histamine is most likely to impair driving ability by causing blurred vision, dizziness, confusion, and loss of coordination.[9]

4.8. UNDESIRABLE EFFECTS

Adverse Effects Associated with Cough Syrup:[7]

Cardiovascular effects	Cardiac dysrhythmia, Hypotension
Dermatologic Effects	Allergic contact dermatitis
Gastrointestinal Effects	Anorexia, Nausea, Vomiting, Epigastric Distress, and Diarrhea or Constipation
Hematologic Effects	Agranulocytosis, Aplastic Anemia, Thrombocytopenia
Neurologic Effects	Dyskinesia, Changes in EEG, Sedation, Somnolence
Psychiatric Effects	Hallucinations
CNS	Drowsiness, dizziness, sedation, confusion, nervousness[8]

4.9. OVERDOSE

Information not available

5. PHARMACOLOGICAL PROPERTIES

Dextromethorphan HBr:

Dextromethorphan Hydrobromide is the hydrobromide salt form of dextromethorphan, a synthetic, methylated dextrorotary analogue of levorphanol, a substance related to codeine and a non-opioid derivate of morphine, one of the active ingredients in many over the counter cold and cough medicines.[2] Dextromethorphan exhibits antitussive activity and is devoid of analgesic or addictive property.[3]

Dextromethorphan has also found other uses in medicine, ranging from pain relief to psychological applications.[4]

Chlorpheniramine:

It is an odorless white crystalline solid or white powder, categorized in first generation antihistamine.

H1 antagonists are agents that antagonize the allergic responses and other effects mediated by histamine. These are also known as *antihistamines*.[6]

Chlorpheniramine is effective in suppressing the flare and wheal effects induced by histamine administration, as well as the allergic symptoms, including pruritus, sneezing, and hypersecretion, associated with pollen allergy. Chlorpheniramine was invariably effective in improving the symptomatology associated with hay fever, allergic rhinitis, conjunctivitis, and all symptoms of seasonal allergic rhinitis except nasal stuffiness.[7]

5.1. PHARMACODYNAMIC PROPERTIES

Dextromethorphan HBr:

Methyl analog of Dextrorphan shows high affinity binding to several regions of the brain, including the medullary cough center. This compound is an NMDA receptor antagonist (N-METHYL-D-ASPARTATE) and acts as a non-competitive channel blocker.

Chlorpheniramine:

Histamine is mainly synthesized in mast cells and basophils of the immune system, enterochromaffin-like cells in gastric mucosa, and certain neurons that release it as a neurotransmitter.

H1-receptor antagonists competitively antagonize histamine at these receptors, mitigating the immune response to an allergen. Many of the first-generation antihistamines also possess anticholinergic activity. This might contribute to some of the side effects associated with these agents, but it also might contribute to their efficacy in the treatment of nausea.[6]

5.2. PHARMACOKINETIC PROPERTIES

Dextromethorphan HBr:

After oral administration, dextromethorphan is quickly absorbed in the gastrointestinal tract with peak serum levels reached within **2-2.5 h**. Dextromethorphan is absorbed from the bloodstream and crosses the blood-brain into the cerebral spinal fluid by approximately **33-80%.**

The antitussive activity of dextromethorphan lasts for approximately **5-6 hours** with plasma half-live of **2-4 hours**. Dextromethorphan is rapidly metabolized by the liver and is O-demethylated to produce its active metabolite dextrorphan. Dextromethorphan is then further N-demethylated and partially conjugated with glucuronic acid and sulfate ions.

Cytochrome P450 in the 2D6 isoenzyme family inactivates dextromethorphan. Dextromethorphan is eliminated renally unchanged or as a demethylated metabolite.[2]

Chlorpheniramine:[7]

Initial Onset Response arises within 30 minutes of administration, while peak response achieved after 1 to 2 hours.

Therapeutic Drug Concentration: 2.3 to 12.1 ng/ml
Time to Peak Concentration: 2 hours.

Absorption: Peak absorption occurs within one-half hour of administration; peak levels occur in 2 hours and gradually fall over the next 46 hours.

Food delays the absorption of chlorpheniramine.

Distribution: Chlorpheniramine is distributed to the central nervous system which is demonstrated by the drowsiness this agent causes. Chlorpheniramine is widely distributed throughout the tissues of the body. In a fatal overdose case, chlorpheniramine was assayed in the brain, lung, kidney, and liver.

Excretion: Approximately 50% of a dose of Chlorpheniramine is excreted in 12 hours as polar and non-polar metabolites with 3% to 18% occurring as unchanged drug.

Half Life: Elimination half-life is 20 hours, half-life is increased in the presence of renal dysfunction and decreased in children.

5.3. PRECLINICAL SAFETY DATA

Information not available

6. PHARMACEUTICAL PARTICULARS

6.1. LIST OF EXCIPIENTS

Sodium Carboxymethyl cellulose 7HF
Glycerine
Dextromethorphan HBR
Sugar granulated USP
Methyl paraben
Sodium benzoate
Potassium sorbate
Sodium saccharine granular
Purified water (filler)
Sodium citrate dihydrate
Ephedrine hydrochloride
Chlorpheniramine maleate
F.D.C. Red no.40
Hydrochloric acid pure
Imit. Wild cherry flav.37
Purified water

6.2. INCOMPATIBILITIES

Information not available

6.3. SHELF LIFE

24 months

6.4. SPECIAL PRECAUTIONS FOR STORAGE

Information not available

6.5. NATURE AND CONTENTS OF CONTAINER

COREX-D Cough Syrup in bottles of 60 ml and 120 ml.

Manufactured by:
Pfizer Pakistan Limited
B-2, S.I.T.E., Karachi-Pakistan.

7. REFERENCES

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