SUMMARY OF PRODUCT CHARACTERISTICS (SPC)

1. NAME OF THE MEDICINAL PRODUCT

COFGEL COUGH SYRUP (Guaifenesin, Dextromethorphan Hydrobromid and chlorphenamine Maleate Syrup)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml contains 100 mg guaifenesin, 10 mg dextromethorphan hydrobromide and 2 mg chlorphenamine maleate.

Excipient(s) with known effect:

Colour: Ponceau 4R

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Syrup

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications:

For relief of coughs and upper respiratory symptoms, including nasal congestion, associated with allergy or the common cold.
Expectorant for the treatment of coughs.

4.2 Posology and Method of Administration:

Adults and children 12 Years of age or Older: Two teaspoonfuls.
Children 6 to 12 years of age: One teaspoonful
Dose may be repeated every 6 hours.
Do not exceed four doses in a 24-Hours period.

4.3 Contraindication:

Patients with hypersensitivity or idiosyncrasy to any of its ingredients.

Antihistamines are contraindicated in patients with narrow angle glaucoma, urinary retention, peptic ulcer and during an asthma attack.

Dextromethorphan should not be used in patients receiving a monoamine oxidase inhibitor (MAOI) or for 2 weeks after stopping the MAOI drug.

4.4 Special Warnings and Precautions for Use:

WARNINGS

Do not exceed recommended dosage.

Antihistamines may cause excitability, especially in children. At doses higher than the recommended dose, nervousness, dizziness or sleeplessness may occur. Administration of dextromethorphan may be accompanied by histamine release and should be used with caution in atopic children.

PRECAUTIONS

General: Before prescribing medication to suppress or modify cough, identify and provide therapy for the underlying cause of the cough and take caution that modification of cough does not increase the risk of clinical or physiologic complications. Dextromethorphan should be used with caution in sedated or debilitated patients and in patients confined to supine positions. Use with caution in patients with hypertension, heart disease, asthma, hyperthyroidism, increased intraocular pressure, diabetes mellitus 1 and prostatic hypertrophy.

Information for Patients:

Avoid alcohol and other CNS depressants while taking this product. Patients sensitive to antihistamines may experience moderate to severe drowsiness. Antihistamines may impair mental and physical abilities required for the performance of potentially hazardous tasks such as driving a vehicle or operating machinery. Patients should be warned accordingly.

Causes of chronic cough should be excluded if symptoms are persistent. Any accompanying symptoms should be actively sought and appropriately investigated/treated. Stop use and ask a healthcare professional if your cough lasts more than 7 days, comes back or is accompanied by a fever, rash, or persistent headache.

Keep out of the sight and reach of children.

Do not exceed recommended dose.

4.5 Interaction with Other Medicinal Products and Other Forms of Interaction:

Antihistamines may enhance the effects of tricyclic antidepressants, barbiturates, alcohol and other CNS depressants. MAO inhibitors prolong and intensify the anticholinergic effects of antihistamines. The cough-suppressant action of dextromethorphan and narcotic antitussives are additive. Dextromethorphan is contraindicated with monoamine oxidase inhibitors (MAOI).

Alcohol

A dose of 10ml of this medicine administered to an adult weighing 70 kg would result in exposure to 3.0 mg/kg of ethanol which may cause a rise in blood alcohol concentration (BAC) of about 0.5 mg/100 ml.
A dose of 10ml of this medicine administered to a child over 12 years of age and weighing 40 kg would result in exposure to 5.4 mg/kg of ethanol which may cause a rise in blood alcohol concentration (BAC) of about 0.9 mg/100 ml.
For comparison, for an adult drinking a glass of wine or 500 ml of beer, the BAC is likely to be about 50 mg/100 ml. Coadministration with medicines containing e.g. propylene glycol or ethanol may lead to accumulation of ethanol and induce adverse effects, in particular in young children with low or immature metabolic capacity.

4.6 Pregnancy and Lactation:

Use in Pregnancy:

Pregnancy Category C. Animal reproduction studies have not been conducted with Cofgel Cough Syrup. It is not known whether these products can cause fetal harm when administered to a pregnant woman or affect reproduction capacity. Give to a pregnant woman only if clearly needed.
If pregnant or breastfeeding, consult a healthcare professional before use.
Although adequate and well-controlled studies in pregnant women have not been performed, the Collaborative Perinatal Project monitored 197 mother-child pairs exposed to guaifenesin during the first trimester. An increased occurrence of inguinal hernias was found in the neonates. However, congenital defects were not strongly associated with guaifenesin use during pregnancy in 2 large groups of mother-child pairs.

Nursing Mothers:

It is not known whether the drugs in Cofgel Cough Syrup are excreted in human milk. Since many drugs are excreted in human milk and because of the potential for serious side effects in nursing infants, a decision should be made whether to discontinue nursing or discontinue the use of these products, taking into account the importance of the drug to the mother.
Guaifenesin is excreted in breast milk in small quantities.

4.7 Effects on Ability to Drive and Use Machines:

No or negligible influence.

4.8 Undesirable Effects:

Antihistamines may cause sedation, dizziness, diplopia, vomiting, diarrhea, dry mouth, headache, nervousness, nausea, anorexia, heartburn, weakness, polyuria and dysuria and, rarely, excitability in children. Urinary retention may occur in patients with prostatic hypertrophy.
Dextromethorphan may cause drowsiness, dizziness and GI disturbance.

Gastrointestinal Disorders
Nausea, vomiting
Immune System Disorders
Hypersensitivity reactions

4.9 Overdose:

No information is available as to specific results of an overdose of Cofgel Cough Syrup. The signs, symptoms and treatments described below are those of H antihistamine, Guaifenesin and dextromethorphan overdose.

Symptoms:

Should antihistamine effects predominate, central action constitutes the greatest danger. In the small child, predominant symptoms are excitation, Nausea and vomiting, hallucination, ataxia, incoordination, tremors, flushed face and fever. Convulsions, fixed and dilated pupils, coma and death may occur in severe cases. In the adult, fever and flushing are uncommon; excitement leading to convulsions and postictal depression is often preceded by drowsiness and coma. Respiration is usually not seriously depressed; blood pressure is usually stable.

Dextromethorphan may cause respiratory depression with a large overdose.

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Treatment:

In case of overdose, discontinue use and seek professional assistance immediately

(a) Evacuate stomach as condition warrants. Activated charcoal may be useful.

(b) Maintain a non stimulating environment. (c) Monitor cardiovascular status. (d) Do not give stimulants. (e) Reduce fever with cool sponging. (f) Treat respiratory depression with naloxone if dextromethorphan toxicity is suspected. (g) Use sedatives or anticonvulsants to control CNS excitation and convulsions. (h) Physostigmine may reverse anticholinergic symptoms. (i) Ammonium chloride may acidify the urine to increase urinary excretion of phenylephrine. (j)

Further care is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties:

Chlorpheniramine maleate possesses H1 antihistaminic activity and mild anticholinergic and sedative effects. Peak plasma concentration is reached in 5 hours. Urinary excretion is the

major route of elimination. The liver is assumed to be the major site of metabolic transformation.

Dextromethorphan hydrobromide is a non-narcotic antitussive with effectiveness equal to codeine. It acts in the medulla oblongata to elevate the cough threshold. Dextromethorphan does not produce analgesia or induce tolerance, and has no potential for addiction. At usual doses, it will not depress respiration or inhibit ciliary activity. Dextromethorphan is rapidly metabolized with trace amounts of the parent compound in blood and urine. About one-half of the administered dose is excreted in the urine as conjugated metabolites.

Guaifenesin has an expectorant action which increases the output of respiratory tract fluid by reducing adhesiveness and surface tension. The increased flow of less viscid secretions promotes ciliary action and facilitates the removal of mucus.
This changes an unproductive cough to a cough that is more productive and less frequent.
Pharmacotherapeutic group: Expectorant
ATC code: RO5CAO3

5.2 Pharmacokinetic Properties:
Guaiphenesin:
Absorption:
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 Cmax was approximately 1.4ug/ml, with tmax occurring approximately 15 minutes after drug administration.
Distribution:
No information is available on the distribution of Guaiphenesin in humans.
Metabolism and elimination:
Guaiphenesin appears to undergo both oxidation and demethylation. Following an oral dose of 600 mg guaifenesin to 3 healthy male volunteers, the t½ 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.

Chlorpheniramine has a serum half-life of approximately 20 hours in adults, and elimination from the body is primarily by metabolism to monodesmethyl and didesmethyl compounds.

Dextromethorphan

Absorption

Dextromethorphan is rapidly absorbed from the gastrointestinal tract with peak plasma concentrations reached in approximately 2 to 2.5 hours. The low plasma levels of dextromethorphan suggest low oral bioavailability secondary to extensive first-pass (pre-systemic metabolism) in the liver. The maximum clinical effects occur 5 to 6 hours after ingestion of dextromethorphan.

Distribution

Dextromethorphan is widely distributed in the human body. Dextromethorphan and its active metabolite, dextrorphan, are actively taken up and concentrated in brain tissue. It is not known if dextromethorphan or dextrorphan are excreted in breast milk or cross the placenta.

Metabolism

Dextromethorphan undergoes rapid and extensive first-pass metabolism in the liver after oral administration. Genetically controlled O-demethylation (CYD2D6) is the main determinant of dextromethorphan pharmacokinetics in human volunteers.

It appears that there are distinct phenotypes for this oxidation process resulting in highly variable pharmacokinetics between subjects. Unmetabolised dextromethorphan, together with the three demethylated morphinan metabolites dextrorphan (also known as 3-hydroxy-N-methylmorphinan), 3- hydroxymorphinan and 3-methoxymorphinan have been identified as conjugated products in the urine.

Dextrorphan, which also has antitussive action, is the main metabolite. In some individuals metabolism proceeds more slowly and unchanged dextromethorphan predominates in the blood and urine.

Excretion

Dextromethorphan is primarily excreted via the kidney as unchanged parent drug and its active metabolite, dextrorphan. Dextrorphan and 3-hydroxy-morphinan are further metabolised by glucuronidation and are eliminated via the kidneys.

The elimination half-life of the parent compound is between 1.4 to 3.9 hours; dextrorphan is between 3.4 to 5.6 hours. The half-life of dextromethorphan in poor metabolisers is extremely prolonged, in the range of 45 hours.

5.3 Preclinical Safety Data:

No further information other than that which is included in the summary product characteristic.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients:

Sucrose
Levomenthol
Sodium methyl Hydroxybenzoate
Sodium Propyl Hydroxybenzoate
Sodium Benzoate
Propylene Glycol
Citric Acid Monohydrate
Flavor cardamom Narda
Colour Ponceau 4R supra
Purified water

6.2 Incompatibilities:

Not applicable

6.3 Shelf Life:

36 Months

6.4 Special Precautions for Storage:

Store below 30^0C in a dry place. Protect from Light.

Keep medicine out of reach of children.

6.5 Nature and Contents of Container:

Primary Packing: 100 ml of Amber coloured Pet bottle

Secondary Packing: Such one bottle with measuring cup is to be packed in printed carton along with pack insert.

6.6 Special Precautions for Disposal and other Handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORIZATION NUMBER

Renewal Registration Number: 07410/07818/VAR/2022

9. DATE OF FIRST AUTHORIZATION / RENEWAL OF AUTHORIZATION

FIRST AUTHORIZATION :24/10/2016

10. DATE OF REVISION OF THE TEXT

12/07/2023

11. REFERENCES