1. Name of medicinal product

Emzolyn cough syrup

2. Qualitative and quantitative composition

Each 5 ml contains:

Diphenhydramine hydrochloride…….14.0 mg

L-menthol……2.0 mg

Each 5ml also contains:

Sucrose……....1 g

Liquid glucose……...…..3.5 g

Ethanol…….197 mg

Ponceau 4R (E 124) ……..0.25 mg

Sodium…….….16.62 mg

Benzyl alcohol……0.22 mg

Sodium benzoate (E 211) ……...…10 mg

For a full list of excipients, see section 6.1.

3. Pharmaceutical form

Syrup.

A clear red syrup

4. Clinical particulars

4.1 Therapeutic indications

Emzolyn Cough Syrup is indicated for the relief of cough and associated congestive symptoms.

4.2 Posology and method of administration

For oral use

Adults and Children aged 12 years and over:

One 10 ml dose of syrup 4 times a day.

Maximum daily dose: 40 ml syrup.

Children under 12 years:

Emzolyn Cough Syrup is contraindicated in children under the age of 12 years (see section 4.3).

The Elderly:

Normal adult dosage is appropriate, [See Pharmacokinetics in the Elderly].

Do not exceed the stated dose.

Keep out of the reach and sight of children.

4.3 Contraindications

Emzolyn Expectorant is contraindicated in individuals with known hypersensitivity to the product or any of its components.

Emzolyn Expectorant is contraindicated in individuals who are taking, or have taken, monoamine oxidase inhibitors within the preceding two weeks. The concomitant use of a dextromethorphan-containing product and monoamine

oxidase inhibitors can occasionally result in symptoms such as hyperpyrexia, hallucinations, gross excitation or coma.

Dextromethorphan, in common with other centrally acting antitussive agents, should not be given to subjects in, orat risk of developing respiratory failure.

Not to be used in children under the age of 12 years.

4.4 Special warnings and precautions for use

This product may cause drowsiness; if affected, individuals should not drive or operate machinery. Diphenhydramine should not be taken by individuals with narrow-angle glaucoma or symptomatic prostatic hypertrophy. Subjects with moderate to severe renal or hepatic dysfunction should exercise caution when using this product (see pharmacokinetics).

4.5 Interaction with other medicinal products and other forms of interaction

The concomitant use of a dextromethorphan-containing product and monoamine oxidase inhibitors can occasionally result in symptoms such as hyperpyrexia, hallucinations, gross excitation or coma. [See Contraindications.]

This product contains diphenhydramine and therefore may potentiate the effects of alcohol, and other CNS depressants.

As diphenhydramine possess some anticholinergic activity, the effects of anticholinergics (e.g. some psychotropic drugs and atropine) may be potentiated by this product. This may result in tachycardia, mouth dryness, gastrointestinal disturbances (e.g. colic), urinary retention and headache.

4.6 Pregnancy and lactation

Both diphenhydramine and dextromethorphan have been in widespread use for many years without apparent ill consequence. However, there is insufficient information on the effects of the administration of dextromethorphan during human pregnancy. In addition, it is not known whether dextromethorphan or its metabolites are excreted in breast milk. Diphenhydramine is known to cross the placenta and has also been detected in breast milk.

Emzolyn Expectorant should therefore only be used when the potential benefit of treatment to the mother exceeds any possible hazards to the developing fetus or suckling infant.

4.7 Effects on ability to drive and use machines

This product may cause drowsiness; if affected, individuals should not drive or operate machinery.

This medicine can impair cognitive function and can affect a patient's ability to drive safely. This class of medicine is in the list of drugs included in regulations under 5a of the Road Traffic Act 1988. When taking this medicine, patients should be told:

- The medicine is likely to affect your ability to drive
- Do not drive until you know how the medicine affects you
- It is an offence to drive while under the influence of this medicine
- However, you would not be committing an offence (called 'statutory defense') if:
    - The medicine has been taken to treat a medical or dental problem and
    - You have taken it according to the information provided with the medicine and
    - It was not affecting your ability to drive safely.

Details regarding a new driving offence concerning driving after drugs have been taken in the UK may be found here: https://www.gov.uk/drug-driving-law

4.8 Undesirable effects

Diphenhydramine may cause: drowsiness; dizziness; gastrointestinal disturbance; dry mouth,

nose and throat; difficulty in urination or blurred vision.

Dextromethorphan: dizziness, nausea, vomiting, or gastro-intestinal disturbance may occur.

Adverse reactions to menthol at the low concentration present in Emzolyn Expectorant are

not anticipated.

4.9 Overdose

Symptoms and signs

The effects of acute toxicity of Emzolyn Expectorant may include drowsiness, hyperpyrexia, anticholinergic effects, lethargy, nystagmus, ataxia, respiratory depression, nausea, vomiting, and hyperactivity. With higher doses, and particularly in children, symptoms of CNS excitation including hallucinations and convulsions may appear; with massive doses, coma or cardiovascular collapse may follow

Treatment

Treatment of overdose should be symptomatic and supportive. Measures to promote rapid gastric emptying (with syrup of ipecac-induced emesis or gastric lavage) and, in cases of acute poisoning, the use of activated charcoal, may be useful. The intravenous use of physostigmine may be efficacious in antagonizing severe anticholinergic symptoms. Naloxone has been used successfully as a specific antagonist to dextromethorphan toxicity in children. Convulsions may be controlled with diazepam and thiopental sodium.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Dextromethorphan

Dextromethorphan is a non-opioid antitussive drug. It exerts its antitussive activity by acting on the cough center in the medulla oblongata, raising the threshold for the cough reflex. A single oral dose of 10-20 mg dextromethorphan produces its antitussive action within 1 hour and lasts for at least 4 hours.

Diphenhydramine

Diphenhydramine possesses antitussive, antihistaminic, and anticholinergic properties. Experiments have shown that the antitussive effect (resulting from an action on the brainstem) is discrete from its antihistaminic effect. The duration of activity of diphenhydramine is between 4 and 8 hours.

Menthol has mild local anesthetic and decongestant properties.

5.2 Pharmacokinetic properties

Absorption

Diphenhydramine, dextromethorphan and menthol are well absorbed from the gut following oral administration. Peak serum levels of diphenhydramine following a 50 mg oral dose are reached at between 2 and 2.5 hours after an oral dose. Due to individual differences in the metabolism of dextromethorphan [See Metabolism & Elimination], pharmacokinetic values are highly variable. After the administration of a 20 mg dose of dextromethorphan to healthy volunteers, the Cmax varied from < 1 µg/l to 8 µg/l, occurring within 2.5 hours of administration.

Distribution

Diphenhydramine

Diphenhydramine is widely distributed throughout the body, including the CNS. Following a 50 mg oral dose of diphenhydramine, the volume of distribution is in the range 3.3 - 6.8 L/kg and it is some 78% bound to plasma proteins.

Dextromethorphan

Due to extensive pre-systemic metabolism by the liver, detailed analysis of the distribution of orally administered dextromethorphan is not possible.

Metabolism and elimination

Diphenhydramine

Diphenhydramine undergoes extensive first pass metabolism. Two successive Ndemethylations occur, with the resultant amine being oxidized to a carboxylic acid. Values for plasma clearance of a 50 mg oral dose of diphenhydramine lie in the range 600 - 1300 ml/min, and the terminal elimination half-life lies in the range 3.4 - 9.3 hours. Little unchanged drug is excreted in the urine.

Dextromethorphan

Dextromethorphan undergoes rapid and extensive first-pass metabolism in the liver after oral administration. Genetically controlled O-demethylation 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. Unmetabolized 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.

Menthol

Menthol is hydroxylated in the liver by microsomal enzymes to p-methane -3,8 diol. This is then conjugated with glucuronide and excreted both in urine and bile as the glucuronide.

Pharmacokinetics in Renal Impairment

The results of a review on the use of diphenhydramine in renal failure suggest that in moderate to severe renal failure, the dose interval should be extended by a period dependent on the glomerular filtration rate (GFR).

There have been no specific studies of Emzolyn Expectorant or dextromethorphan in renal impairment.

Pharmacokinetics in Hepatic Impairment

After intravenous administration of 0.8 mg/kg diphenhydramine, a prolonged half-life was noted in patients with chronic liver disease which correlated with the severity of the disease. However, the mean plasma clearance and apparent volume of distribution were not significantly affected

There have been no specific studies of Emzolyn Cough Syrup or dextromethorphan in hepatic impairment.

Pharmacokinetics in the Elderly

Pharmacokinetic studies indicate no major differences in distribution or elimination of diphenhydramine compared to younger adults.

There have been no specific studies of Emzolyn Expectorant or dextromethorphan in the elderly.

5.3 Preclinical safety data

The active ingredients of Emzolyn Expectorant are well-known constituents of medicinal products and their safety profiles are well documented. The results of pre-clinical studies do not add anything of relevance for therapeutic purposes.

6. Pharmaceutical particulars

6.1 List of excipients

- Liquid glucose
- Sucrose
- Ethanol (96%)
- Glycerol
- Sodium citrate
- Saccharin sodium
- Citric acid monohydrate
- Sodium benzoate
- Caramel T12
- Raspberry flavor 503.850/T
- Carbomer
- Ponceau 4R (E124)
- Purified water

6.2 Incompatibilities

None known

6.3 Shelf life

3 years

6.4 Special precautions for storage

Do not store above 30°C. Store in the original container.

6.5 Nature and contents of container

125 or 150 ml amber glass bottles with a 2 piece or a 3 piece plastic child resistant, tamper

evident closure fitted with a polyterephtalate ethylene faced aluminum/expanded polyethylene laminated wad

6.6 Special precautions for disposal and other handling

None applicable.

7. Marketing authorization holder

Emzor Pharmaceutical Industries Limited

No 10, Kolawole, Shonibare Street, Ajao Estate, Isolo, Lagos Nigeria.

8. Marketing authorization number(s)

N/A

9. Date of first authorization/renewal of authorization

N/A

10. Date of revision of text

5/12/2024.