SUMMARY OF PRODUCT CHARACTERISTICS (SPC)

TRIMEX SYRUP

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1. NAME OF THE MEDICINAL PRODUCT

Trimex Syrup

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Chlorpheniramine Maleate BP 2.0 mg
Pseudoephedrine HCl 30.0 mg
Guaifenesin BP 100.0 mg

3. PHARMACEUTICAL FORM

Liquid (Syrup)

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Trimex cough expectorant is indicated for the effective relief from chesty coughs by assisting in the loosening and removal of stubborn bronchial mucus. Its additional ingredients also assist to clear nasal congestion associated with chesty coughs.

4.2. Posology and method of administration

Adults and children

Over 12 years: One to two

Children

6-12 years half to one

Below 2 years: OnDoctor's advice

4.3. Contraindications

Trimex Expectorant is contra-indicated in patients who have previously exhibited intolerance to it or any of its constituents or in patients who are taking or have taken mono-amine oxidase inhibitors within the preceding two weeks. It is also contra-indicated in patients with severe hypertension and coronary heart disease.

4.5 Interaction with other medicinal products and other forms of interaction

Caution should be exercised with patients receiving other sympathomimetic agents (e.g. avoid use with apraclonidine), appetite suppressants or other amphetamine -like psychostimulants, as there is a risk of hypertension.
Pseudoephedrine may antagonise the effects of antihypertensive agents, such as adrenergic neurone blockers, and severe hypertension may occur in patients receiving beta-blockers.
Hypertensive crisis may occur if pseudoephedrine is co-administered with MAOIs. Concomitant use of pseudoephedrine should be avoided with MAOIs including rasagiline and selegiline, or RIMAs such as moclobemide.
There may be increased risk of arrhythmias if pseudoephedrine is given to patients receiving cardiac glycosides, quinidine, volatile anaesthetics such as cyclopropane, or halothane, or anticholinergic drugs such as tricyclic antidepressants. Pseudoephedrine also increases the risk of ergotism if used with ergot alkaloids, ergotamine and methysergide.
The effects of pseudoephedrine may be antagonized by antipsychotics and its absorption rate may be reduced by kaolin.
The effects of pseudoephedrine may be increased by doxapram and oxytocin (as there is a risk of hypertension) and its absorption may be increased by aluminium hydroxide.
The antibacterial agent furazolidone is known to cause progressive inhibition of monoamine oxidase (a metabolite of furazolidone is a MAOI). Although there have been no reports of hypertensive crisis, it may not be administered concurrently with pseudoephedrine.

Alcoholic drinks and certain other central nervous system depressants such as anxiolytics or hypnotics can potentiate the sedative effects of Chlorphenamine.
Phenytoin metabolism is inhibited by Chlorphenamine and this can cause phenytoin toxicity.
The anticholinergic effects of Chlorphenamine are intensified by the use of other anticholinergic drugs such as atropine, tricyclic antidepressants and MAOI's (see contraindications).
If urine is collected within 24 hours of a dose of Trimex Adult Syrup a metabolite of guaifenesin may cause a colour interference with laboratory determinations of urinary 5-hydroxyindoleacetic acid (5-HIAA) and vanillylmandelic acid (VMA).

4.6 Pregnancy and lactation

There are limited data from the use of pseudoephedrine in pregnant women. It is advised that pseudoephedrine should be avoided during pregnancy, particularly during the first trimester, as defective closure of the abdominal wall (gastroschisis) has been reported very rarely in new-borns after first trimester exposure.
Pseudoephedrine has been detected in human milk with a small percentage of the total maternal dose potentially administered to the suckling infant. The use of pseudoephedrine should be avoided during breast feeding as lactation may be suppressed, and irritability and disturbed sleep have been reported in breast fed infants.

4.7 Effects on ability to drive and use machines

Trimex expectorant may cause drowsiness and patients should not drive or operate machinery, if affected avoid alcohol.

4.8 Undesirable effects

Dryness of the mouth, throat and nose, abdominal pain with vomiting and diarrhea, central nervous system (CNS) depressant activity, gastrointestinal disturbances, hypersensitivity reaction, blood disorders, ventricular arrhythmias, paradoxical CNS stimulation, sleep disturbances and skin rashes

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

Pseudoephedrine has direct and indirect sympathomimetic activity and is an orally effective upper respiratory decongestant. Pseudoephedrine is substantially less potent than ephedrine in producing both tachycardia and elevation in systolic blood pressure and considerably less potent in causing stimulation of the central nervous system.
Guaifenesin is thought to exert its pharmacological action by stimulating receptors in the gastric mucosa. This increases the output from secretory glands of the gastrointestinal system and reflexly increases the flow of fluids from glands lining the respiratory tract. The result is an increase in volume and decrease in viscosity of bronchial secretions. Other actions may include stimulating vagal nerve endings in bronchial secretory glands and stimulating certain centres in the brain, which in turn enhance respiratory fluid flow. Guaifenesin produces its expectorant action within 24 hours.
Chlorphenamine is a potent H_1 – blocking drug. Antihistamines diminish or abolish the actions of histamine in the body by competitive reversible blockade of the histamine H_1-receptor sites in tissues. Chlorphenamine also has an anticholinergic activity.
Antihistamines act to prevent the release of histamine, prostaglandins and leukotrines and have been shown to prevent the migration of inflammatory mediators. The actions of chlorphenamine include the inhibition of histamine on smooth muscle, capillary permeability and therefore reduction of oedema and wheal in hypersensitivity reactions such as allergy and anaphylaxis.

5.2 Pharmacokinetic properties

Chlorphenamine maleate is absorbed relatively slowly from the gastrointestinal tract and peak plasma concentrations occur between 2.5 and 6 hours after oral administration. It is reported that only 25 to 50% of an oral dose is absorbed as it appears that chlorphenamine undergoes considerable first pass metabolism. Metabolites include desmethyl- and didesmethylchlorphenamine. Chlorphenamine distributes widely in the body and penetrates into the CNS. In the circulation, about 70% of chlorphenamine is bound to plasma proteins.
Excretion of unchanged drug and metabolites is mainly via the urine and is dependent on urinary pH and flow rate. The elimination half-life is widely variable and has been reported to range from 2 to 43 hours. However, the duration of action is only 4-6 hours which is shorter than might be predicted.
It is reported that in children, absorption is faster and more extensive, and there is a quicker clearance with a shorter half-life.

Absorption

Guaifenesin 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 guaifenesin to healthy adult volunteers, the C_{max} was approximately 1.4 ug/ml, with t_{max} occurring approximately 15 minutes after drug administration.

Distribution

No information is available on the distribution of guaifenesin in humans.

Metabolism and elimination

Guaifenesin 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 Trimex Syrup orguaifenesin in subjects with renal or hepatic impairment.
Caution is therefore recommended when administering this product to subjects with severe renal or hepatic impairment.

Pharmacokinetics in the Elderly

Not applicable.

Pseudophedrine hydrochloride is readily and completely absorbed from the gastro-intestinal tract. It is resistant to metabolism by monoamine oxidase and is largely excreted unchanged in the urine.

5.3 Preclinical safety data

Mutagenicity

There is insufficient information available to determine whether guaifenesin has mutagenic potential.

Carcinogenicity

There is insufficient information available to determine whether guaifenesin has carcinogenic potential.

Teratogenicity

There is insufficient information available to determine whether guaifenesin has teratogenic potential.

Fertility

There is insufficient information available to determine whether guaifenesin has the potential to impair fertility.

6. PHARMACEUTICAL PARTICULARS

6.1. List of ingredients

- Methyl paraben
- Menthol
- Hydroxyethyl Cellulose
- Citric acid anhydrous
- Propyl paraben
- Sucrose
- Sodium Saccharin
- Potassium Sorbate
- Purified Water.
- Alcohol 90%(Rectified Spirit)
- Vanilla Flavor Liquid
- Strawberry Flavor
- Sunset Yellow FD & Yellow 6 colour.

6.2. **Incompatibilities**

Not applicable.

6.3. **Shelf life**

36 months

6.4. **Special precautions for storage**

Store below 30^0 C, in a dry place. Protect from light keep out of reach of children.

Legal category:

General Sale Medicine

6.5 Nature and contents of container

Glass amber bottle, unit carton

6.6Special precautions for disposal and other handling

No special requirements.

7. **REGISTRANT**

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