1. Name of the medicinal product

Trimex mucolytic syrup

2. Qualitative and quantitative composition

Each 5mls contains: Salbutamol sulphate BP 2.4mg.
Bromhexine HCL 4.0mg
Guaifenesin 100.0mg

3. Pharmaceutical form

Oral syrup.

Orange yellow coloured clear viscous syrup free from visible impurities.

4. Clinical particulars

4.1 Therapeutic indications
Trimex mucolytic is indicated for the effective relief from bronchitis and bronchial asthma. It helps in increased respiration by bronchodilation in cases productive coughs.

4.2 Posology and method of administration
Adults and children above 12 years: 10mls (2 teaspoons), to be taken three times a day.

Children 6-12 years 5mls (1 teaspoon), to be taken three times a day.

2-6 years 2.5mls (1/2 teaspoon), to be taken three times a day.

Not recommended for children below 2 years of age or as directed by a doctor.

4.3 Contraindications
Known hypersensitivity to the components of trimex mucolytic syrup.

Trimex mucolytic is contraindicated 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 oxide inhibitors within the preceding two weeks. It is also contra-indicated in patients with severe heart hypertension and coronary heart disease.

4.4 Special warnings and precautions for use
It should be taken with caution in patients with cardiac disorders, hypertension and peptic ulcers.
Do not give with a cough suppressant.
Caution should be exercised in the presence of severe renal or severe hepatic impairment.
Not more than 4 doses should be given in any 24 hours. Do not exceed the stated dose.
Do not take with any other cough and cold medicine.
Patients with rare hereditary problems of fructose intolerance should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction
Caution should be exercised in its use with anaesthetic agents such as chloroform, cyclopropane, halothane and other halogenated agents.
Salbutamol is not contraindicated in patients under treatment with monoamine oxidase inhibitors (MAOIs).
If urine is collected within 24 hours of a dose of Trimex mucolytic 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

Pregnancy

There is little published evidence of its safety in the early stages of human pregnancy, but in animal studies there was evidence of some harmful effects on the foetus at very high dose levels.

Lactation

Bromhexine is probably excreted into breast milk and should be avoided during breastfeeding.
As salbutamol is probably secreted in breast milk its use in nursing mothers requires careful consideration.
Guaifenesin is excreted in breast milk in small amounts. There is insufficient information on the effects of Guaifenesin in breastfed newborns/infants.

A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Trimex mucolytic syrup therapy, taking into account the benefit of breast -feeding for the child and the benefit of therapy for the woman.

4.7 Effects on ability to drive and use machines

Dizziness may occur during treatment.

4.8 Undesirable effects

The safety of guaifenesin is based on available data from clinical trials and adverse drug reactions (ADRs) identified during post-marketing experience.

The frequencies are provided according to the following convention:

Very common ≥1/10

Common ≥1/100 and < 1/10

Uncommon ≥1/1,000 and <1/100

Rare ≥1/10,000 and <1/1,000

Very rare <1/10,000

Not known (cannot be estimated from the available data)

Body system (SOC)	Incidence	Adverse Event Preferred Term
Immune system disorders	Not known	Hypersensitivity reactions (hypersensitivity, pruritus and urticaria) Rash
Gastrointestinal disorders	Not known	Abdominal pain upper Diarrhoea Nausea Vomiting

a) Summary of the safety profile

The most common side effect of Salbutamol is fine tremor of the hands, which may interfere with precise manual work. Tension, restlessness and a rapid heart-beat may also occur. There have been very rare reports of muscle cramps. Hypersensitivity reactions such as angioedema, urticaria, bronchospasm, hypotension and collapse have rarely been reported. Potentially serious hypokalaemia may result from β_2-agonist therapy. Occasional headaches have also been reported. As with other drugs in this class rare reports of hyperactivity in children have been reported.

b) Tabulated list of adverse reactions

Adverse events are listed below by system organ class and frequency. Frequencies are defined as: very common (≥1/10), common (≥1/100 and <1/10), uncommon (≥1/1000 and <1/100), rare (≥1/10,000 and <1/1000) and very rare (<1/10,000) including isolated reports. Very common and common events were generally determined from clinical trial data. Rare, very rare and unknown events were generally determined from spontaneous data.

Immune system disorders	
Very rare:	Hypersensitivity reactions including angioedema, urticaria, bronchospasm, hypotension and collapse.
Metabolism and nutrition disorders	
Rare:	Hypokalaemia.
Potentially serious hypokalaemia may result from beta agonist therapy.	
Nervous system disorders	
Very common:	Tremor.
Common:	Headache.
Very rare:	Hyperactivity.
Cardiac disorders	
Common:	Tachycardia, palpitations.
Rare:	Cardiac arrhythmias including atrial fibrillation, supraventricular tachycardia and extrasystoles
Unknown:	Myocardial ischaemia* (see section 4.4)
Vascular disorders	
Rare:	Peripheral vasodilatation.
Musculoskeletal and connective tissue disorders	
Common:	Muscle cramps.
Very rare:	Feeling of muscle tension.

* reported spontaneously in post-marketing data therefore frequency regarded as unknown.

The undesirable effects are classified by system organ system and frequency. The frequency is classified as follows: Very common (≥ 1/10), Common (≥ 1/100 to < 1/10), Uncommon (≥ 1/1,000 to < 1/100), Rare (≥ 1/10,000 to < 1/1,000), Very rare (< 1/10,000), not known (cannot be estimated from the available data)

Frequency/ System Organ Class	Common	Uncommon	Rare	Not known
Immune system disorders			Hypersensitivity reactions	Anaphylactic reactions including anaphylactic shock, angioedema and puritus
Psychiatric disorders	Anxiety	Insomnia	Hallucinations, confusion, aggressiveness	
Nervous system disorders	Tremor			
Cardiac disorders	Palpitations			
Respiratory, thoracic and mediastinal disorders			Bronchospasm	
Gastrointesinal disorders		Nausea, diarrhoea and vomiting	Dry mouth	Reduced appetite
Skin and subcutaneous tissue disorders	Urticaria, rash			Severe cutaneous adverse reactions (including erythema multiforme, Stevens-Johnson syndrome/ toxic epidermal necrolysis and acute generalized exanthematous pustulosis)
Renal and urinary tract disorders	Difficulty in micturition, urinary retention			
General disorders and administration site conditions	Dizziness, headache			
Investigations			Transaminase increase	

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

4.9 Overdose

Symptoms: Nausea and vomiting

Treatment: gastric lavage, general supportive measures.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Trimex mucolytic is a combination of 3 active ingredients:

Guaifenesin increases the volume and reduces viscosity of tenacious sputum and is used as an expectorant for productive cough. 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.

Salbutamol sulphate is a direct acting sympathomimetic with predominant beta-adrenergic activity, and acts as a bronchodilator. As a beta-adrenergic stimulant for relief of bronchospasm such as occurs with asthma, bronchitis, emphysema. It has a highly selective action on the receptors in bronchial muscle and in therapeutic dosage, little or no action on the cardiac receptors.

Bromhexine is a mucolytic used in the treatment of respiratory disorders associated with productive cough. Bromhexine hydrochloride is considered to have an expectorant and mucolytic effect that dissolves sticky secretions. This may facilitate the expectoration of mucus.

5.2 Pharmacokinetic properties

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.
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.

Salbutamol is readily absorbed from the gastro-intestinal tract and is subject to first pass metabolism in the liver. Peak plasma concentrations occur within one to four hours after oral administration. After multiple oral doses of salbutamol 4mg four times a day, steady-state plasma concentrations are obtained after 3 days. About half is excreted in the urine as an inactive sulphate conjugate following oral administration. The bioavailability of orally administered salbutamol is about 50%.

Bromhexine hydrochloride is rapidly absorbed, and the maximum plasma concentration is reached after about an hour. Bromhexine hydrochloride undergoes extensive first-pass metabolism, and the oral bioavailability is approximately 20%. There is a high degree of protein binding. 85–90% of bromhexine hydrochloride is eliminated as metabolites in urine, with a terminal half-life of up to 12 hours. Only a small fraction is eliminated unchanged in the urine, with a half-life of 6.5 hours.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC

6. Pharmaceutical particulars

6.1 List of excipients
Menthol, Methyl Paraben, Propyl paraben, Sucrose, Hydroxyethyl Cellulose (Natrosol HHX250), Potassium sorbate, Sunset Yellow FD&C Yellow 6 Colour (E110), Propylene glycol, Aspartame, Strawberry Flavour, Citric Acid Anhydrous, Glycerin, Alcohol 90% (Rectified Spirit), Purified water.

6.2 Incompatibilities
None Stated.

6.3 Shelf life
Bottles: 36 months

6.4 Special precautions for storage
None