PROFESSIONAL INFORMATION

SCHEDULING STATUS

S2

1. NAME OF THE MEDICINE

DURO-TUSS LINCTUS, 2,41 milligrams, 4 milligrams Liquid

2. QUALITATIVE AND QUANTITATIVE COMPOSTION

Each 5 ml liquid contains: Salbutamol sulphate 2,41 mg

Bromhexine hydrochloride 4 mg

Preservative: Sodium Benzoate 0,2 % *m/v*

Sugar free.

Contains sweetener (sucralose 2,5 mg /5 ml).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Liquid

A clear, colourless, slightly viscous liquid with an odour of orange.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

DURO-TUSS LINCTUS is indicated for the relief of cough associated with bronchospasm (wheezing).

4.2 Posology and method of administration

Posology

Adults: 10 ml three to four times a day

Children 6 – 12 years: 5 ml three to four times a day

Children 2 – 6 years:2,5 ml – 5 ml three to four times a day

Do not exceed the recommended dose.

Suitable for children, elderly and diabetics.

4.3 Contraindications

DURO-TUSS LINCTUS is contra-indicated in:

- Patients with known hypersensitivity to salbutamol, bromhexine or to any other ingredients in DURO-TUSS LINCTUS listed in section 6.1.
- Patients with cardiac dysrhythmias or tachycardia.
- Patients receiving monoamine oxidase inhibitors (MAOI's) or within 14 days of MAOI's termination.

4.4 Special warnings and precautions for use

Salbutamol Sulphate

Use with caution in hyperthyroidism, myocardial insufficiency, susceptibility to QT-interval prolongation, hypertension, diabetes mellitus, and in severe asthma.

Bronchodilators should not be the only or main treatment in patients with severe or unstable asthma. Severe asthma requires regular medical assessment including lung function testing as patients are at risk of severe attacks and even death. Medical practitioners should consider using oral corticosteroid therapy and/or the maximum recommended dose of inhaled corticosteroid in those patients.

The dosage or frequency of administration should only be increased on medical advice.

The management of asthma should normally follow a stepwise programme, and patient response should be monitored clinically and by lung function tests.

Increasing use of bronchodilators in particular short-acting inhaled beta$_2$-agonists to relieve symptoms indicates deterioration of asthma control. The patient should be instructed to seek medical advice if short-acting relief bronchodilator treatment becomes less effective or they need more inhalations than usual.

In this situation patients should be reassessed, and consideration given to the need for increased anti-inflammatory therapy (e.g. Higher doses of inhaled corticosteroids or a course of oral corticosteroid). Severe exacerbations of asthma must be treated in the normal way.

Patients should be warned that if either the usual relief with DURO-TUSS LINCTUS oral preparations is diminished or the usual duration of action reduced, they should not increase the dose or its frequency of administration but should seek medical advice.

Cardiovascular effects may be seen with sympathomimetic drugs, including salbutamol. There is some evidence from post-marketing data and published literature of rare occurrences of myocardial ischaemia associated with salbutamol. Patients with underlying severe heart disease (e.g. ischaemic heart disease, dysrhythmia or severe heart failure) who are receiving salbutamol should be warned to seek medical advice if they experience chest pain or other symptoms of worsening heart disease. Attention should be paid to assessment of symptoms such as dyspnoea and chest pain, as they may be of either respiratory or cardiac origin.

Plasma-potassium concentrations should be monitored in severe asthma as hypokalaemia may occur. The risk can be potentiated by hypoxia and acidosis, or the concomitant use with other medicines that cause hypokalaemia or cardiac dysrhythmias. (see sections 4.5 and 4.8)

High doses may increase the risk of serious side effects, including cardiac dysrhythmias, the maximum dose should not be exceeded.

Salbutamol as contained in DURO-TUSS LINCTUS should be administered cautiously to patients suffering from thyrotoxicosis.

In common with other β-adrenoceptor agonists, DURO-TUSS LINCTUS can induce reversible metabolic changes such as increased blood glucose levels. Diabetic patients may be unable to compensate for the increase in blood glucose and the development of ketoacidosis has been reported. Concurrent administration of corticosteroids can exaggerate this effect.

Bromhexine hydrochloride

Use with care in patients with a history of peptic ulceration. The inhibition of the cough reflex by the simultaneous administration of codeine or another antitussive may lead to a build-up of secretion in patients with strong secretion formation, which is associated with the risk of bronchospasm and - due to the inhibition of self-cleaning of the airways - a respiratory tract infection.

If a serious respiratory disease is suspected (e.g. high fever for 3 days or cough for more than a week), a doctor should be consulted to clarify the underlying disease and rule out a malignant pathology.

If hypersensitivity reactions occur, the treatment should be stopped immediately and a doctor should be consulted if necessary.

Very rare cases of temporally associated serious skin damage such as Stevens Johnson syndrome and toxic epidermal necrolysis (TEN, Lyell's syndrome) have been reported with the administration of expectorant substances such as bromhexine. In most cases, these could be explained by the severity of the underlying disease or the concomitant use of another medicine. In the early stages of such severe skin reactions, only unspecific flu-like symptoms, such as fever, body aches, runny nose, cough and sore throat, can initially occur.

If new skin or mucous membrane damage occurs, medical advice should be obtained immediately and treatment with DURO-TUSS LINCTUS should be discontinued as a precautionary measure.

Care is also advisable in asthmatic patients.

Clearance of bromhexine or its metabolites may be reduced in patients with severe hepatic or renal impairment.

4.5 Interaction with other medicines and other forms of interaction

Salbutamol Sulphate

Concomitant administration of DURO-TUSS LINCTUS with sympathomimetics, diuretics, corticosteroids or xanthines e.g. theophylline, increases the risk of hypokalaemia. (see section 4.4 above)

DURO-TUSS LINCTUS and non-selective beta-blocking medicines, such as propranolol, should not usually be prescribed together.

Bromhexine hydrochloride

The simultaneous administration of non-steroidal anti-inflammatory drugs (e.g. diclofenac, ibuprofen, salicylates) can cause a mutual intensification of the gastric mucosal irritant effects.

The simultaneous use of DURO-TUSS LINCTUS and certain antibiotics (e.g. erythromycin) improves the transfer of the antibiotics into the lung tissue.

After using bromhexine (e.g. DURO-TUSS LINCTUS), the concentrations of the antibiotics amoxicillin, erythromycin and oxytetracycline in the sputum and bronchial secretions are increased.

4.6 Fertility, pregnancy and lactation

Pregnancy

The safety of DURO-TUSS LINCTUS in pregnant women has not been established.

DURO-TUSS LINCTUS may delay onset of labour.

Small amounts of bromhexine cross the placenta.

Breastfeeding

The safety of DURO-TUSS LINCTUS in lactating women has not been established.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

The following side effects have been reported:

Salbutamol Sulphate

Immune system disorders

Less frequent	Hypersensitivity reactions including angioedema, urticaria, including paradoxical bronchospasm, hypotension and collapse
Metabolism and nutrition disorders	
Less frequent	Hyperglycaemia. Hypokalaemia that may be potentiated by concomitant therapy with corticosteroids, diuretics, or xanthines and by hypoxia and acidosis. (see section 4.4)
Nervous system disorders	
Frequent	Tremor, headache and nervous tension
Less frequent	Hyperactivity
Frequency unknown	Hallucinations in children, restlessness
Cardiac disorders	
Frequent	Tachycardia due to increased sympathetic effects on the cardiovascular system, palpitations
Less frequent	Cardiac dysrhythmias including atrial fibrillation, supraventricular tachycardia and extrasystoles
Frequency unknown	Myocardial ischaemia (see section 4.4)
Vascular disorders	
Less frequent	Peripheral vasodilation with flushing
Frequency unknown	Hypotension
Musculoskeletal and connective tissue disorders	
Frequent	Muscle cramps
Less frequent	Feeling of muscle tension

Bromhexine hydrochloride

Immune system disorders	
Less frequent	Hypersensitivity
Frequency unknown	Anaphylactic reactions up to anaphylactic shock

Gastrointestinal disorders	
Less frequent	Upper abdominal pain, nausea, vomiting, diarrhoea
Hepato-biliary disorders	
Frequency unknown	Transient rise in serum aminotransferase values
Respiratory, thoracic and mediastinal dysfunction	
Frequency unknown	Bronchospasm
Skin and subcutaneous tissue disorders	
Less frequent	Skin rashes
Frequency unknown	Angioedema, urticaria, pruritus
General disorders and administrative site conditions	
Frequency unknown	Headache, dizziness, sweating

4.9 Overdose

See section 4.8. Salbutamol overdosage may result in tachycardia, central nervous system stimulation, tremor, hypokalaemia and hyperglycaemia. Treatment is symptomatic and supportive. Activated charcoal may be considered in patients who present within 1 hour of overdosage.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A.10.1 Antitussives and expectorants.

Salbutamol sulphate

Salbutamol is a β_2-selective adrenergic bronchodilator. It acts by stimulating β_2-adrenergic receptors in the lungs to relax bronchial smooth muscle.

The onset of action is within 30 minutes, with a peak effect between 2 to 3 hours after the dose, and a duration of action of up to 6 hours.

Bromhexine hydrochloride

Bromhexine hydrochloride reduces the viscosity of non-infected secretions from mucous cells in the respiratory tract, *in vitro*.

5.2 Pharmacokinetic properties

Salbutamol sulphate

Salbutamol is readily absorbed from the gastrointestinal tract. It is subject to first pass metabolism in the liver and possibly in the gut wall. The main metabolite is an inactive sulphate conjugate. It is excreted in the urine as metabolites and unchanged salbutamol, and some is excreted in the faeces. The plasma half-life of Salbutamol has been estimated to range from 4 to 6 hours.

Bromhexine hydrochloride

Bromhexine hydrochloride is well absorbed from the gastrointestinal tract with peak plasma concentrations after about 1 hour. Bromhexine undergoes extensive first-pass metabolism in the liver, with a bioavailability of about 20 %. It is widely distributed to body tissues. About 85 % to 90 % of a dose is excreted in the urine mainly as metabolites, including ambroxol. Bromhexine is highly bound to plasma proteins. It has a terminal elimination half-life of 13 to 40 hours. Bromhexine crosses the blood-brain barrier and small amounts cross the placenta.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Benzoate 0,2 % *m/v* (as preservative)

Citric acid anhydrous

Hydroxyethylcellulose

Menthol

Orange flavour

Propylene glycol

Purified water

Sucralose

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at or below 30 °C. Protect from light.

6.5 Nature and contents of container

Amber plastic (PET) bottles containing 100 ml and 200 ml. The bottles are packed in a printed unit carton.

7. HOLDER OF CERTIFICATE OF REGISTRATION

iNova Pharmaceuticals (Pty) Ltd

15e Riley Road

Bedfordview

South Africa

8. REGISTRATION NUMBER

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of registration: 10 August 2007

10. DATE OF REVISION OF TEXT

26 August 2021