Applicant/PHCR:	Ranbaxy Pharmaceuticals (Pty) Ltd
Product proprietary name:	BETALIX DECONGESTANT
Dosage form and strength:	Elixir; Each 5 ml contains chlorpheniramine maleate 2 mg, phenylephrine hydrochloride 2,5 mg, phenylpropanolamine hydrochloride 2,5 mg
Date of amendment:	July 2021

1.5.5 Proposed Professional Information

SCHEDULING STATUS

S2

1. NAME OF THE MEDICINE

BETALIX DECONGESTANT elixir

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml contains:

Chlorpheniramine maleate 2 mg

Phenylpropanolamine hydrochloride 2,5 mg

Phenylephrine hydrochloride 2,5 mg

Preserved with sodium benzoate 0,2 % *m/v*

Contains sugar: Sorbitol solution 70 % 3,5 ml per 5 ml

Contains no alcohol.

For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Elixir

A sweet, light green, cream-soda flavoured elixir.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For the symptomatic relief of nasal congestion associated with colds and flu, hay fever, allergic rhinitis, other upper respiratory allergies, or associated with sinusitis.

Relief of Eustachian tube congestion as an adjunct to treatment of middle ear infection.

4.2 Posology and method of administration

Children 6 – 12 years: One 5 ml medicine measureful 3 or 4 times daily.

Children 2 – 6 years: Half a 5 ml medicine measureful 3 or 4 times daily.

4.3 Contraindications

- Hypersensitivity to chlorpheniramine maleate, phenylpropanolamine hydrochloride, phenylephrine hydrochloride, or to any of the excipients listed in section 6.1.
- Coronary disease, hypertension, cardiovascular disease, hyperthyroidism and during acute asthma attacks.
- Patients being treated with monoamine oxidase inhibitors or within 2 weeks of stopping such treatment.
- Diabetes mellitus.
- Pregnancy and lactation.
- Children under the age of two years.

4.4 Special warnings and precautions for use

BETALIX DECONGESTANT should not be taken for more than seven days. After 5 to 7 days tachyphylaxis may occur and the product loses effect. If symptoms do not improve, or are accompanied by fever, consult a doctor.

Exceeding the recommended dosage may result in nervousness, dizziness, sleeplessness; tremulousness or cardiac dysrhythmia. This may also occur in sensitive individuals at small doses.

Severe hypertensive episodes leading to intracranial haemorrhage have followed phenylpropanolamine ingestion. Patients should be informed of the dangers of exceeding the recommended dose; in particular the increased risk of serious adverse effects such as hypertensive crisis and haemorrhagic stroke. Patients with cardiovascular disease, hypertension or hyperthyroidism should not use **BETALIX DECONGESTANT** (see section 4.3). In addition, **BETALIX DECONGESTANT** may aggravate conditions such as diabetes, glaucoma or prostatic enlargement. Patients on monoamine oxidase inhibitors (e.g. tranylcypromine) should not use **BETALIX DECONGESTANT** (see section 4.3).

BETALIX DECONGESTANT should be used with care in conditions such as narrow angle glaucoma, urinary retention and prostatic hypertrophy.

BETALIX DECONGESTANT should be used with caution in patients who may be hyper-susceptible to their effects, particularly those with hyperthyroidism. Great care is also needed in patients with cardiovascular disease such as ischaemic heart disease, arrhythmia or tachycardia; occlusive vascular disorders, including arteriosclerosis, hypertension or aneurysms.

Anginal pain may be precipitated in patients with angina pectoris. Care is also required when **BETALIX DECONGESTANT** is given to patients with diabetes mellitus or closed-angle glaucoma.

Sorbitol

BETALIX DECONGESTANT contains sorbitol 70 % solution and may cause gastrointestinal discomfort and have a mild laxative effect. Patients with hereditary fructose intolerance (HFI) should not take/be given **BETALIX DECONGESTANT**.

4.5 Interaction with other medicines and other forms of interaction

Chlopheniramine maleate

Monoamine oxidase inhibitors may enhance the antimuscarinic effects of chlorpheniramine and chlorpheniramine has an additive antimuscarinic action.

With other antimuscarinic medicines, such as atropine and tricyclic antidepressants, cholrpheniramine may enhance the sedative effects of central nervous system depressants including alcohol, barbiturates, hypnotics, narcotic analgesics, sedatives and tranquillisers. Patients should abstain from alcohol.

Chorpheniramine may mask the warning signs of damage caused by oxotoxic medicines such as aminoglycoside antibiotics.

Chlorphenamine inhibits phenytoin metabolism leading to phenytoin toxicity.

Cholrpheniramine may suppress positive skin test results and should be stopped several days before the test.

Phenylephrine and phenylpropanolamine

Phenylephrine and phenylpropanolamine should be avoided or used with caution in patients undergoing anaesthesia with cylcopropane, halothane or other halogenated anaesthetics, as they may induce ventricular fibrillation.

An increased risk of arrhythmias may also occur if sympathomimetic medicines are given to patients receiving cardiac glycosides, quinidine or tricyclic antidepressants.

Reversal of the action of many antihypertensive medicines occurs in patients given phenylephrine and phenylpropanolamine and therefore special care is advisable in patients receiving antihypertensive therapy. Interactions with alpha- and beta- blocking medicines may be complex.

4.6 Fertility, pregnancy and lactation

BETALIX DECONGESTANT is contraindicated in pregnancy and lactation.

Phenylephrine hydrochloride is best avoided in pregnancy, because of the potential promotion of uterine contractility and peripheral vasoconstriction, with the possibility of foetal hypoxia.

4.7 Effects on the ability to drive and use machines

BETALIX DECONGESTANT leads to drowsiness, which is aggravated by the simultaneous intake of alcohol and other central nervous system depressants. Patients so affected should not drive or operate machinery.

4.8 Undesirable effects

Chlorpheniramine maleate		
System Order Class	**Frequency**	**Side effect**
Blood and the lymphatic system disorders	Less frequent	Agranulocytosis, leucopaenia and haemolytic anaemia
Psychiatric disorders	Less frequent	Depression, nightmares, irritability
	Frequency unknown	Euphoria
Nervous system disorders	Frequent	Sedation varying from slight drowsiness to deep sleep, and including lassitude, dizziness
	Less frequent	Incoordination, headache, impaired concentration
Eye disorders	Less frequent	Blurred vision
Ear and labyrinth disorders	Less frequent	Tinnitus
Cardiac disorders	Less frequent	Palpitation, tachycardia, dysrhythmia
Vascular disorders	Less frequent	Hypotension
Respiratory, thoracic and mediastinal disorders	Less frequent	Increased viscosity of bronchial secretions
Gastrointestinal disorders	Less frequent	Nausea, vomiting, diarrhoea or constipation, anorexia or increased appetite, abdominal pain, dyspepsia, dryness of the mouth and epigastric pain

Hepato-biliary disorders	Less frequent	Hepatitis, jaundice
Skin and subcutaneous tissue disorders	Less frequent	Allergic reactions including exfoliative dermatitis and cross-sensitivity to related medicines may occur, photosensitivity and skin reactions such as urticaria
Musculoskeletal, connective tissue and bone disorders	Less frequent	Muscular weakness, twitching
Renal and urinary disorders	Less frequent	Urinary retention
	Frequency unknown	Difficulty in micturition, dysuria
General disorders and administrative site conditions	Less frequent	Tightness of the chest Paradoxical central nervous system stimulation may occur, especially in children, with insomnia, nervousness, tachycardia, tremors and convulsions

Phenylpropanolamine		
System Order Class	**Frequency**	**Side effect**
Psychiatric disorders	Frequency unknown	Fear, anxiety, restlessness, tremor, insomnia, confusion, irritability, weakness and psychotic states
Gastrointestinal disorders	Frequency unknown	Nausea, vomiting, appetite may be reduced, hypersalivation
Metabolism and nutritional disorders	Frequency unknown	Altered metabolism including disturbances of glucose metabolism

Phenylephrine		
System Order Class	**Frequency**	**Side effect**
Psychiatric disorders	Frequent	Nervousness, irritability, restlessness, and excitability
	Frequency unknown	Fear, anxiety, tremor, insomnia, confusion, weakness and psychotic states
Nervous system disorders	Frequent	Headache, dizziness, insomnia
Eye disorders	Frequency unknown	Mydriasis, acute angle closure glaucoma
Cardiac disorders	Frequency unknown	Tachycardia or bradycardia, cardiac dysrhythmias, angina pain, palpitations, cardiac arrest
Vascular disorders	Frequent	Increased blood pressure
	Frequency unknown	Hypotension with dizziness, tainting and flushing may occur, haemorrhagic stroke, flushing, sweating, vasoconstriction
Respiratory, thoracic and mediastinal disorders	Frequency unknown	Dyspnoea
Gastrointestinal disorders	Frequent	Nausea, vomiting, diarrhoea
	Frequency unknown	Appetite may be reduced, hypersalivation
Metabolism and nutritional disorders	Frequency unknown	Altered metabolism including disturbances of glucose metabolism

Skin and subcutaneous tissue disorders	Frequency unknown	Allergic reactions such as rash, urticaria, allergic dermatitis, hypersensitivity reactions, including cross-sensitivity with other sympathomimetics
Renal and urinary disorders	Frequency unknown	Difficulty in micturition, urinary retention, dysuria

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the '**6.04 Adverse Drug Reaction Reporting Form**', found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/index/8

4.9 Overdose

Symptoms

Chlorpheniramine maleate

Overdosage may be fatal especially in infants and children in whom the main symptoms are central nervous system stimulation and antimuscarinic effects, including ataxia, excitement, hallucinations, muscle tremor, convulsions, dilated pupils, dry mouth, flushed face and hyperpyrexia. Deepening coma, cardiorespiratory collapse, and death may occur within 18 hours. In adults, the usual symptoms are of central nervous system depression with drowsiness, coma and convulsions. Hypotension may also occur. Elderly patients are more susceptible to the central nervous system depressant and hypotensive effects even at therapeutic doses.

Phenylpropanolamine

Overdosage of phenylpropanolamine may cause giddiness, headache, nausea, vomiting, sweating, thirst, palpitations, difficulty in micturition, muscular weakness and tremors, anxiety, restlessness and insomnia. Overdosage may also cause psychoses, hallucinations and cardiorespiratory collapse. Severe increase in blood pressure may occur.

Phenylephrine

Overdosage with phenylephrine may cause headache, hypertension, palpitations and vomiting. Severe increase In blood pressure may occur.

Treatment

Treatment with alpha-adrenergic blocking medicines to reduce blood pressure should be instituted if myocardial ischaemia or encephalopathy is provoked. Further treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 5.8 Preparations for the common cold including nasal decongestants

Mechanism of action

The combination has antihistaminic and sympathomimetic properties.

Chlorpheniramine is an antihistamine with sedative properties.

Phenylephrine is a sympathomimetic amine which acts directly on alpha-adrenergic receptors. It is without significant stimulating effects on the central nervous system at usual doses.

Phenylpropanolamine is a sympathomimetic amine which acts directly by displacing noradrenaline from pre-synaptic stores. It has some direct effects on both alpha- and beta-adrenergic receptors with predominantly alpha-adrenergic activity. The sympathomimetic amines have alpha-adrenergic receptor stimulating properties on the mucosa of the respiratory tract producing vasoconstriction.

5.2 Pharmacokinetic properties

Chlorpheniramine maleate is absorbed relatively slowly from the gastrointestinal tract and peak plasma concentrations occur about 2,5 to 6 hours after oral doses. Bioavailability is low, values of 25 to 50 % have been reported. Chlorpheniramine appears to undergo considerable first-pass metabolism. About 70 % of chlorpheniramine in the circulation is bound to plasma proteins. Chlorpheniramine is widely distributed in the body and enters the CNS. Chlorpheniramine is extensively metabolised. Metabolites include desmethyl- and didesmethylchlorpheniramine. Unchanged chlorpheniramine and its metabolites are excreted mainly in the urine; excretion is dependent on urinary pH and flow rate. Only trace amounts have been found in the faeces. More rapid and extensive absorption, faster clearance and a shorter half-life have reported in children.

Phenylpronolamine is readily and completely absorbed from the gastrointestinal tract and peak plasma concentrations occur about 1 to 2 hours after oral doses. It undergoes some metabolism in the liver, to an active hydroxylated metabolite, but up to 80 to 90% of a dose is excreted unchanged in the urine within 24 hours. The half-life has been reported to be about 3 to 5 hours.

Phenylephrine has a low bioavailability owing to irregular absorption and first-pass metabolism by monoamine oxidase in the gut and liver.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Brilliant blue (CI 42090)

Citric acid anhydrous

Sodium benzoate

Sorbitol solution 70 %

Sunset yellow (CI 15985)

Purified water

Quinolene yellow (CI 47005)

Trusil cream soda

Xanthan gum

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store in a cool place at or below 25 °C and protect from light.

6.5 Nature and contents of container

Amber glass or HDPE bottles containing 100 ml and 200 ml. Sealed with a white tamper-evident closure.

6.6 Special precautions for disposal and other handling

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

7. HOLDER OF CERTIFICATE OF REGISTRATION

Ranbaxy Pharmaceuticals (Pty) Ltd

14 Lautre Road

Stormill Ext. 1

Roodepoort 1724

South Africa

8. REGISTRATION NUMBER(S)

28/5.8/0648

Namibia: NS1 04/5.8/0994

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

25 November 1994

10. DATE OF REVISION OF THE TEXT

Will be allocated by SAHPRA upon approval of update