SCHEDULING STATUS

S2

1. NAME OF THE MEDICINE

TRIFEN® EXPECT PAEDIATRIC solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml contains:

Pseudoephedrine hydrochloride 12 mg

Codeine phosphate 3 mg

Triprolidine hydrochloride 0,6 mg

Guaiphenesin 50 mg

Preservatives

Methyl hydroxybenzoate 0,12 % *m/v*

Propyl hydroxybenzoate 0,02 % *m/v*

Contains propyl gallate 0,05 % *m/v*

Contains sugar:

Liquid glucose: 1 g/5 ml

Sorbitol 70 % solution: 1,29 g/ 5 ml

Contains sweetener: Saccharin sodium: 5 mg/5 ml

For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Solution

Clear red solution with raspberry odour and taste.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

TRIFEN® EXPECT PAEDIATRIC is indicated for the alleviation of cough.

4.2 Posology and method of administration

Children 6 to 12 years – 5 ml to 10 ml

Children 2 to 5 years – 2,5 ml to 5 ml

May be given three times daily.

4.3 Contraindications

- Hypersensitivity to pseudoephedrine hydrochloride, codeine phosphate, triprolidine hydrochloride, guaiphenesin or to any of the excipients listed in section 6.1.
- Cardiovascular disease,
- Hypertension.
- Thyrotoxicosis.
- Bladder dysfunction.
- Narrow angle glaucoma.
- Phaeochromocytoma.
- Patients being treated with monoamine oxidase inhibitors and within two weeks of stopping such treatment.
- Ephedrine and other sympathomimetic medicines as a hypertensive response may result.
- During the acute attack of bronchial asthma.
- Head injuries and where the intracranial pressure is raised.

- Heart failure secondary to chronic lung disease.
- Respiratory failure, especially in the presence of cyanosis and excessive bronchial secretion.
- Children under the age of 2 years.

4.4 Special warnings and precautions for use

Exceeding the prescribed dose, together with prolonged and continuous use of this medication, may lead to dependency and addiction.

Pseudoephedrine HCl should be given with caution to patients with organic heart disease, cardiac decompensation or angina of effort. In patients with prostatic enlargement, it may cause difficulty with micturition.

TRIFEN® EXPECT PAEDIATRIC should be used with caution in patients with aneurisms, cardiac arrhythmias (e.g. tachycardia), diabetes mellitus and occlusive vascular disorders (arteriosclerosis). Tolerance may develop when given to asthmatics for their asthmatic effects.

Large doses may precipitate fits in epileptics.

Codeine should be used with caution in patients with obstructive bowel disorders, liver impairment, myasthenia gravis, prostatic hypertrophy, impaired renal function or shock. It should be used with caution or in reduced doses in patients with adrenocortical insufficiency and hypothyroidism.

Dosages should be reduced in debilitated and elderly patients.

TRIFEN® EXPECT PAEDIATRIC may interfere with diagnostic measurements of 5-hydroxy-indoleacetic acid and vanillylmandelic acid.

Excipients

TRIFEN® EXPECT PAEDIATRIC contains which may have an effect on the glycaemic control of patients with diabetes mellitus. Patients with rare glucose-galactose malabsorption should not take/be given **TRIFEN® EXPECT PAEDIATRIC**.

TRIFEN® EXPECT PAEDIATRIC contains sorbitol 70 % solution. Patients with hereditary fructose intolerance (HFI) should not take/be given **TRIFEN® EXPECT PAEDIATRIC**.

4.5 Interaction with other medicines and other forms of interaction

TRIFEN® EXPECT PAEDIATRIC should be used with caution in patients taking other sympathomimetic medicines, such as decongestants, appetite suppressants and amphetamine-like psycho-stimulants, or antihypertensive medicines, as this may cause a rise in blood pressure largely, because of interaction with pseudoephedrine HCl.

The effect of a single dose of **TRIFEN® EXPEC PAEDIATRIC** on the blood pressure of these patients should be observed before recommending repeated or unsupervised treatment.

The antibacterial medicine, furazolidone, is known to cause a dose related inhibition of monoamine oxidase. **TRIFEN® EXPECT PAEDIATRIC** and furazolidone should not be taken together.

The effects of **TRIFEN® EXPECT PAEDIATRIC** due to pseudoephedrine HCl, are diminished by guanethidine, reserpine, methyldopa and may be diminished by tricyclic antidepressants.

The effects of atropine and tricyclic antidepressants may be enhanced by triprolidine HCl.

Triprolidine may enhance the central nervous system sedative effects of alcohol, barbiturates, hypnotics, narcotic analgesics, sedatives and tranquillisers. Triprolidine HCl may mask the warning symptoms of damage caused by ototoxic drugs and may affect the metabolism of medicines in the liver.

Codeine may affect the activity of other medicines by delaying their absorption. The depressant effects of codeine are aggravated by alcohol, anaesthetics, hypnotics and sedatives, tricyclic antidepressants and phenothiazines.

Chronic ingestion of anticonvulsants and oral steroid contraceptives induces liver enzymes and may prevent attainment of therapeutic levels by increasing first past metabolism or clearance.

4.6 Fertility, pregnancy and lactation

The safety of **TRIFEN® EXPECT PAEDIATRIC** during pregnancy and lactation has not been established.

4.7 Effects on the ability to drive and use machines

The use of **TRIFEN® EXPECT PAEDIATRIC** may lead to drowsiness and impaired concentration which may be aggravated by the simultaneous intake of alcohol or other central nervous system depressants.

Patients should be warned against taking charge of vehicles, or operating machinery where loss of concentration may lead to accidents.

4.8 Undesirable effects

	Trifen Expect Paediatric			
	Pseudoephedrine hydrochloride	**Codeine phosphate**	**Triprolidine hydrochloride**	**Guaiphenesin**
Blood and the lymphatic system disorders:				
Frequency unknown			Blood dyscrasias, agranulocytosis, haemolytic anaemia	
Immune system disorders:				
Frequency unknown			Allergy, anaphylaxis	
Metabolism and nutrition disorders:				
Frequency unknown	Thirst, loss of appetite, disturbance of glucose metabolism, dry mouth	Dry mouth	Anorexia, dry mouth	
Psychiatric disorders:				
Frequency unknown	Anxiety, insomnia, confusion, fear, psychotic states, irritability, restlessness, agitation	Confusion, drowsiness, euphoria, mood changes, restlessness	Elation or depression, irritability, nightmares	
Nervous system disorders:				
Frequent			Sedation varying from slight drowsiness to deep sleep	
Frequency unknown	Giddiness, headache, pre-cordial pain, tremors, dizziness, cerebral haemorrhage	Deepening coma, increased intracranial pressure	Inability to concentrate, lassitude, dizziness, incoordination, headache, tingling, heaviness and weakness of the hands	
Eye disorders:				
Frequency unknown		Miosis		
Ear and labyrinth disorders:				

Frequency unknown		Vertigo	Tinnitus	
Cardiac disorders:				
Frequency unknown	Palpitation, tachycardia, hypertension, ventricular arrhythmias, reflex bradycardia, cardiac arrest, dyspnoea**,** vasoconstriction which may result in hypertension, pulmonary oedema	Bradycardia, circulatory failure, hypotension, orthostatic hypotension, palpitations	Hypotension, tightness of the chest	
Vascular disorders:				
Frequency unknown	Weakness	Flushing		
Respiratory, thoracic and mediastinal disorders:				
Frequency unknown		Respiratory depression		
Gastrointestinal disorders:				
Less Frequent		Increased risk of abdominal pain, including pancreatitis		
Frequency unknown	Nausea, vomiting	Nausea, vomiting, constipation	Nausea, vomiting, diarrhoea, constipation, epigastric pain	Gastrointestinal discomfort, nausea, vomiting
Skin and subcutaneous tissue disorders:				
Frequency unknown	Fixed drug eruption, taking the form of erythematous nummular patches	Pruritus, urticaria	Lichenoid skin eruption	
Musculoskeletal, connective tissue and bone disorders:				
Frequency unknown	Muscular weakness	Muscle rigidity	Muscular weakness	
Renal and urinary disorders:				
Frequency unknown	Difficulty with micturition	Urinary retention, ureteric and biliary spasm, antidiuretic effect	Difficulty with micturition	
General disorders and administrative site conditions:				

Frequency unknown	Sweating, fainting, blushing	Sweating, hypothermia		

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 of overdosage with codeine phosphate include the following: nausea, vomiting, restlessness, sensory disturbances, muscle tremor, diuresis, palpitations, stupor, shock, central stimulation with exhilaration, convulsions, drowsiness, respiratory depression, hypotension with circulatory failure, respiratory collapse, cyanosis and coma.

In acute poisoning the stomach should be emptied by aspiration and lavage. Intensive supportive therapy may be necessary to correct respiratory failure and shock. The specific antagonist naloxone may be used to counteract severe respiratory depression.

Symptoms of pseudoephedrine HCl overdosage may include paranoid psychosis, delusions and hallucinations.

Further treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacological classification: A.10.1 Anti-tussives and expectorants

Mechanism of action

Pseudoephedrine has direct and indirect sympathomimetic activity and is an effective upper respiratory decongestant.

Triprolidine is a potent, competitive histamine H1-receptor antagonist. Being an alkylamine, triprolidine possesses minimal anticholinergic activity. Triprolidine provides symptomatic relief in conditions believed to depend wholly, or partly, upon the triggered release of histamine.

Codeine is metabolized by the liver enzyme CYP2D6 into morphine, its active metabolite, which is an agonist of opiate receptors and possesses analgesic, antitussive, and antidiarrheal actions.

Guaiphenesin 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.

5.2 Pharmacokinetic properties

After absorption from the gastrointestinal tract, triprolidine is metabolised; a carboxylated derivative accounts for about half the dose excretedin the urine. Reported half-lives vary from 3 to 5 hours or more. Triprolidine is distributed into breast milk.

Pseudoephedrine is readily absorbed from the gastrointestinal tract. It is excreted largely unchanged in the urine with small amounts of its hepatic metabolite. It has a half-life about 5 to 8 hours; elimination is enhanced and half-life accordingly shorter in acid urine. Small amounts are distributed into breast milk.

Guaiphenesin is well absorbed from the gastrointestinal tract. It is metabolised and then excreted in the urine.

Codeine and its salts are absorbed from the gastrointestinal tract. Ingestion of codeine phosphate produces peak plasma-codeine concentrations in about one hour. Codeine is metabolised by O- and N-demethylation in the liver to morphine, norcodeine, and other metabolites including normorphine and hydrocodone. Metabolism to morphine is mediated by the cytochrome P450 isoenzyme CYP2D6, which shows genetic polymorphism. Codeine and its metabolites are excreted almost entirely by the kidney, mainly as conjugates with glucuronic acid. The plasma half-life has been reported to be between 3 and 4 hours after oral dose. Codeine crosses the placenta and is distributed into breast milk.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Citric acid monohydrate

Liquid glucose

Methyl hydroxybenzoate

Propyl hydroxybenzoate

Purified water

Raspberry red H1277 (C.I. no. 14720)

Raspberry special essence

Propyl gallate

Saccharin sodium

Sodium citrate

Sorbitol 70 %

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at or below 25 °C and protect from light.

6.5 Nature and contents of container

100 ml and 200 ml amber glass bottles.

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)

27/10.1/0536 (South Africa)

Zambia: P168/014

Namibia: NS1 04/19.1/1006

Malawi: PMPB/PL4/29

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

05 October 1993

10. DATE OF REVISION OF THE TEXT

13 March 2023