1.3.1.1 Professional Information for Medicines for Human Use

SCHEDULING STATUS:

S2

1. **Name of the medicine**

   INNOSPECT PAEDIATRIC (SYRUP)

2. **Qualitative and Quantitative composition**

   INNOSPECT PAEDIATRIC

   Triprolidine hydrochloride: 0,6 mg

   Pseudoephedrine hydrochloride: 12,0 mg

   Codeine Phosphate: 3,0 mg

   Guaiphenesin:50,0 mg

   Contains sugar:

   Glucose liquid: 250 mg

   sucrose: 1,325 mg

   Glycerol: 0,250 ml.

   'For full list of excipients, see section 6.1'

3. **Pharmaceutical form**

Syrup. A bright red syrup with the odour and taste of raspberry.

4. **Clinical particulars**

4.1 therapeutic indications:

INNOSPECT is indicated ~~F~~for the alleviation of cough.

4.2 Posology and method of administration

Children:

6 to 12 years: Take 5 ml to 10 ml three times a day.

2 to 5 years: Take 2,5 ml to 5 ml three times a day.

Peadiatric population

INNOSPECT is contraindicated in children under two years of age.

Method of administration

INNOSPECT should be taken orally.

4.3 Contraindications

- Patients with hypersensitivity to the active ingredients or to any of the excipients in INNOSPECT (see section 6.1)
- Children under two years of age
- Patients using other sympathomimetic decongestants or beta-blockers.
- Pregnancy and lactation (see section 4.6)
- Comatose patients
- Patients with respiratory depression, especially in the presence of cyanosis and excessive bronchial secretion
- Acute alcoholism
- Head injuries and conditions in which intracranial pressure is raised ~~and~~
- After operations on the biliary tract.
- Conditions where inhibition of peristalsis is to be avoided.
- Where there is a risk of paralytic ileus.

- Acute diarrhoeal conditions such as acute ulcerative colitis or antibiotic associated colitis (e.g. pseudomembranous colitis).
- Paediatric patients (2 to 18 years of age) who undergo tonsillectomy and/or adenoidectomy for obstructive sleep apnoea syndrome.
- Adolescents (12 to 18 years) who have problems with breathing (see section 4.4).
- Patients known to be CYP2D6 ultra-rapid metabolisers.
- Patients with liver disease or severe hepatic dysfunction.
- Patients with:
  - coronary thrombosis,
  - severe or uncontrolled high blood pressure
  - severe or acute chronic kidney disease
  - Diabetes
  - hyperthyroidism,
  - closed-angle glaucoma ~~and~~
  - hyper-excitability,
  - phaeochromocytoma,
  - urinary retention
  - prostatic hypertrophy
- In persons under treatment with monoamine oxidase inhibitors, or within two weeks of stopping treatment.
- Patients with cardiovascular disease including ischaemic heart disease, and ocular vascular disease

4.4 Special warning and precautions for use

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

Triprolidine HCL

- Triprolidine, as contained in **INNOSPECT**, may lead to drowsiness and impaired concentration that may be aggravated by the simultaneous intake of alcohol or other central nervous system depressants. Patients should be advised, particularly at the initiation of therapy, against taking charge of vehicles or machinery or performing potentially hazardous tasks where loss of concentration could lead to accidents.
- Because of the antimuscarinic actions of triprolidine, as contained in **INNOSPECT**, **INNOSPECT** should be used with care in conditions such as angle-closure glaucoma, urinary retention, prostatic hyperplasia, or pyloroduodenal obstruction.
- **INNOSPECT** should be used with caution in patients with epilepsy, hepatic and renal impairment.
- Elderly patients are more susceptible to many of the adverse effects of an antihistamines such as triprolidine as contained in **INNOSPECT**.
- Triprolidine HCl, as contained in **INNOSPECT**, may mask the warning symptoms of damage caused by ototoxic medicines and may affect the metabolism of medicines in the liver.

Pseudoephedrine HCl

- **INNOSPECT** should be given with caution to patients with organic heart disease, cardiac decompensation or angina. In patients with prostatic enlargement, it may cause difficulty with micturition.
- Pseudoephedrine HCl, as contained in **INNOSPECT** increases the risk of posterior reversible encephalopathy syndrome (PRES) and reversible cerebral vasoconstriction syndrome (RCVS) (See section 4.8).
- **INNOSPECT** should not be used in patients with severe or uncontrolled high blood pressure.
- **INNOSPECT** should not be used in patients with acute or chronic kidney disease/failure.
- **INNOSPECT** is contraindicated in patients with severe hepatic impairment (see section 4.3).
- If any of the following occur, **INNOSPECT** should be stopped:
  - Hallucinations.
  - Restlessness.
  - Sleep disturbances.

Guaiphenesin

- **INNOSPECT** should not be used for persistent cough such as that which occurs with smoking, asthma, emphysema or where cough is accompanied by excessive secretions except under the advice and supervision of a doctor.

- A persistent cough may be a sign of a serious condition. If cough persists for more than one week, tends to recur or is accompanied by high fever, rash or persistent headache, consult a medical practitioner.
- Guaiphenesin, as contained in **INNOSPECT**, may interfere with diagnostic measurements of 5 hydroxy-indole acetic acid and vanillylmandelic acid.

Codeine phosphate

- Use with caution in patients with a history of drug abuse. Discontinuation should be gradual in patients who may have developed physical dependence to avoid precipitating withdrawal symptoms.
- Use with caution or in reduced doses in asthma and decreased respiratory reserve, avoid use during an acute asthma attack (see section 4.3).
- INNOSPECT should only be used with caution or in reduced dose in elderly patients or debilitated patients, or in patients with:
  - Hypotension
  - Hypothyroidism
  - Prostatic hypertrophy
  - Adrenocortical insufficiency
  - Inflammatory or obstructive bowel disorders
  - Urethral stricture
  - Shock
  - Convulsive disorders
  - Myasthenia gravis.

- **INNOSPECT** should be avoided, or the dose reduced in patients with renal or hepatic impairment (see section 4.3).
- Codeine, as contained in **INNOSPECT**, should be avoided in patients with biliary tract disorders or used in conjunction with an antispasmodic.
- Codeine, as contained in **INNOSPECT**, is metabolised by the liver enzyme CYP2D6 into morphine, its active metabolite. If a patient has a deficiency or is completely lacking this enzyme an adequate analgesic effect will not be obtained. however, if the patient is an extensive or ultrarapid metaboliser there is an increased risk of developing side effects of opioid toxicity even at commonly prescribed doses. These patients convert codeine into morphine rapidly resulting in higher than expected serum morphine levels. General symptoms of opioid toxicity include confusion, somnolence, shallow breathing, small pupils, nausea, vomiting, constipation and lack of appetite. In severe cases this may include symptoms of circulatory and respiratory depression, which may be life-threatening and fatal.
- Codeine, as contained in **INNOSPECT**, is not recommended for use in children in whom respiratory function might be compromised including neuromuscular disorders, severe cardiac or respiratory conditions, upper respiratory or lung infections, multiple trauma or extensive surgical procedures. These factors may worsen symptoms of morphine toxicity (see section 4.3)

Excipients

- **INNOSPECT** contains glucose and sucrose which may have an effect on the glycaemic control of patients with diabetes mellitus.

- **INNOSPECT** contains sorbitol and may cause gastrointestinal discomfort and mild laxative effect.

4.5 Interaction with other medicines and other forms of interaction

  - *Triprolidine HCl*

- Central nervous system depressants: **INNOSPECT** may enhance the sedative effects of CNS depressants including alcohol, barbiturates, hypnotics, opioid analgesics, anxiolytic sedatives, tranquillisers and antipsychotics.
- Anticholinergics: **INNOSPECT** has an additive anticholinergic action with other anticholinergic medicines, such as atropine and some antidepressants (both tricyclics and MAOIs).
- Aminoglycoside antibacterials: Some sedating antihistamines such as triprolidine, as contained in **INNOSPECT**, could mask the warning signs of damage caused by ototoxic medicines such as aminoglycoside antibacterials.
- Allergen tests: Antihistamines such as triprolidine, as contained in **INNOSPECT**, may suppress the cutaneous histamine response to allergen extracts and should be stopped several days before skin testing.
- Long term use of anticonvulsants and oral steroid contraceptives cause an increase in the first pass metabolism or clearance rate and may prevent attainments of therapeutic levels.

  - *Pseudoephedrine HCl*

- Caution should be exercised with patients receiving other sympathomimetic medicines (e.g. avoid use with apraclonidine), appetite suppressants or other amphetamine -like psychostimulants, as there is a risk of hypertension.
- **INNOSPECT** may antagonise the effects of antihypertensive medicines, such as adrenergic neurone blockers, and severe hypertension may occur in patients receiving beta-blockers.
- Hypertensive crisis may occur if **INNOSPECT** is co-administered with MAOIs. Concomitant use should be avoided with MAOIs (see section 4.3).
- There may be increased risk of dysrhythmias if **INNOSPECT** is given to patients receiving cardiac glycosides, quinidine, volatile anaesthetics such as cyclopropane, or halothane, or anticholinergic medicines such as tricyclic antidepressants.
- **INNOSPECT** also increases the risk of ergotism if used with ergot alkaloids, ergotamine and methysergide.
- The effects of **INNOSPECT** may be antagonised by antipsychotics and its absorption rate may be reduced by kaolin.
- The effects of **INNOSPECT** 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 medicine, furazolidone is known to cause a dose related inhibition of monoamine oxidase.
- **INNOSPECT** and furazolidone should not be taken together.
- The effects of **INNOSPECT** due to pseudoephedrine HCl are diminished by guanethidine, reserpine and methyldopa.

Guaiphenesin

- Interferes with urine tests for 5-hydroxyndoleacetic acid (5-HIAA) and vanillylmandelic acid.

Codeine phosphate

- Alcohol: The hypotensive, sedative and respiratory depressive effects of alcohol may be enhanced.
- Anaesthetics: Concomitant administration of codeine and anaesthetics may cause increased CNS depression and/or respiratory depression and/or hypotension.
- Anti-dysrhythmics: Codeine delays the absorption of mexiletine. The analgesic activity of codeine is likely to be significantly impaired by quinidine which impairs codeine metabolism.
- Antidepressants: The depressant effects of codeine may be enhanced by tricyclic antidepressants.
- MAOIs taken with pethidine have been associated with severe CNS excitation or depression (including hypertension or hypotension). A similar interaction with codeine may occur and therefore the use of codeine should be avoided while the patient is taking MAOIs and for 2 weeks after MAOI discontinuation (see section 4.3).
- Antihistamines: Concomitant administration of codeine and antihistamines with sedative properties may cause increased CNS depression and/or respiratory depression and/or hypotension.
- Antipsychotics: Enhanced sedative and hypotensive effect.
- Anxiolytics and hypnotics: Enhanced sedative effect.

- Domperidone and metoclopramide: Codeine antagonises the effect of cisapride, metoclopramide and domperidone on gastrointestinal activity.
- Ulcer-healing medicines: Cimetidine may inhibit the metabolism of codeine resulting in increased plasma concentrations.
- Interference with laboratory tests: Opioids may interfere with gastric emptying studies as they delay gastric emptying and with hepatobiliary imaging using technetium Tc 99m disofenin as opioid treatment, including codeine treatment, may cause constriction of the sphincter of Oddi and increase biliary tract pressure.

4.6 Fertility, pregnancy, and lactation

The use of **INNOSPECT** is contraindicated in pregnancy and lactation (see section 4.3).

Pregnancy

The safety of **INNOSPECT** in pregnancy has not been established (see section 4.3).

Breastfeeding

The safety of **INNOSPECT** in lactation has not been established (see section 4.3).

Fertility

No data available

4.7 Effects on the ability to drive and use machines.

INNOSPECT has moderate influence. Since adverse reactions such as drowsiness, dizziness, sedation and blurred vision have been reported in patients receiving **INNOSPECT**, patients should not drive, use machinery or perform any tasks that require concentration, until they are certain that **INNOSPECT** does not adversely affect their ability to do so (see section 4.8).

4.8 Undesirable effects

Tabulated summary of adverse reactions

System organ class	Frequency	Side effects
Blood and the lymphatic system disorders	Less frequent	Blood disorders, including, agranulocytosis, leucopenia, haemolytic anaemia, and thrombocytopeni a
Immune system disorders	Frequency unknown	Hypersensitivity reactions including bronchospasm, angioedema, anaphylaxis, cross-sensitivity to related medicines
Psychiatric disorders	Frequency unknown	Confusion, paradoxical stimulation especially at high doses and in children or the elderly, sleep disturbances, depression, nightmares
Nervous system disorders	Frequent	Sedation varying from slight drowsiness to deep sleep, lassitude, dizziness, incoordination, headache, psychomotor impairment, inability to concentrate.
	Frequency unknown	Convulsions, paraesthesia, extrapyramidal effects,

		tremor, elation, irritability
Eye disorders	Frequent	Blurred vision
Ear and labyrinth disorders	Frequency unknown	Tinnitus
Cardiac disorders	Less frequent	Palpitations, dysrhythmias
Vascular disorders	Frequency unknown	Hypotension, hypertension
Respiratory, thoracic and mediastinal disorders	Frequent Frequency unknown	Thickened respiratory-tract secretions. Tightness of chest
Gastrointestinal disorders	Frequent Less frequent Frequency unknown	Dry mouth, constipation, increased gastric reflux. Nausea, vomiting, diarrhoea, epigastric pain. Anorexia
Skin and subcutaneous tissue disorders	Frequency unknown	Rash, sweating, hair loss, lichenoid skin eruption

Musculoskeletal and connective tissue disorders	Frequency unknown	Myalgia, muscular weakness
Renal and urinary disorders	Frequent	Urinary difficulty, urinary retention

Pseudoephedrine HCL

System order class	**Frequency**	**Side effects**
Immune system disorders	Frequency unknown	Hypersensitivity reactions – cross- sensitivity may occur with other sympathomimetics
Metabolism and nutrition disorders	Frequency unknown	Loss of appetite
Psychiatric disorders	Less frequent Frequency unknown	Psychotic disorders due to misuse. Hallucinations (particularly in children), insomnia, sleep disturbances, anxiety, irritability, excitability, agitation, confusion, fear

	Nervous system disorders	Frequency unknown	Restlessness, headache, tremor, dizziness, fainting, cerebral haemorrhage
	Eye disorders	Frequency unknown	Angle-closure glaucoma
	Cardiac disorders	Frequency unknown	Tachycardia, palpitations, dysrhythmia, reflex bradycardia, cardiac arrest, dyspnoea
	Vascular disorders	Frequency unknown	Hypertension, impaired circulation to the extremities, vasoconstriction, blushing
	Respiratory, thoracic and mediastinal disorders	Frequency unknown	Pulmonary oedema
	Gastrointestinal disorders	Frequency unknown	Nausea, vomiting, dry mouth
	Skin and subcutaneous tissue disorders	Frequency unknown	Fixed drug eruption in the form of erythematous nodular patches, rash
	Renal and urinary disorders	Frequency unknown	Urinary retention
	General disorders and	Frequency unknown	Weakness

administrative site conditions		
Cerebral disorders	Frequency unknown	Posterior reversible encephalopathy (PRES), reversible vasoconstriction syndrome (RCVS).

Guaiphenesin

System organ class	Frequent	Side effects
Nervous system disorders	Less frequent Frequency unknown	Headache, Dizziness Drowsiness
Gastrointestinal disorders	Less frequent Frequency unknown	Diarrhoea, nausea, vomiting, stomach pains Discomfort
Skin and Subcutaneous tissue disorders	Less frequent	Rash, urticaria

Codeine phosphate

Regular prolonged use of codeine is known to lead to addiction and tolerance.

Symptoms of restlessness and irritability may result when treatment is then stopped.

Tolerance and some of the most common side effects – drowsiness, nausea, vomiting, and confusion – generally develops with long term use.

System organ class	**Frequent**	**Side effects**
Immune system disorders	Frequency unknown	Maculopapular rash has been seen as part of a hypersensitivity syndrome associated with oral codeine phosphate; fever, splenomegaly and lymphadenopathy also occurred
Metabolism and nutrition disorders	Frequency unknown	Hyperglycaemia, anorexia
Psychotic disorders	Frequency unknown	Mental depression, hallucinations, nightmares, restlessness, confusion, mood changes, euphoria, dysphoria

	Nervous system disorders	Frequency unknown	Convulsions (especially in infants and children), dizziness, drowsiness, headache (prolonged use of a painkiller for headaches can make them worse). Raised intracranial pressure may occur in some patients
	Eye system disorders	Frequency unknown	Blurred or double vision or other changes in vision, miosis
	Ear and labyrinth disorders	Frequency unknown	Vertigo
	Cardiac disorders	Frequency unknown	Tachycardia, palpitations, bradycardia
	Vascular disorders	Frequency unknown	Postural hypotension, facial flushing. Hypotension
	Respiratory, thoracic and mediastinal disorders	Frequency unknown	Dyspnoea. Respiratory depression
	Gastrointestinal disorders	Frequency unknown	Nausea, vomiting, constipation, dry mouth, stomach cramps, pancreatitis

Hepato -biliary disorders	Frequency unknown	Biliary spasm (may be associated with altered liver enzyme values)
Skin and subcutaneous tissue disorders	Frequency unknown	Allergic reactions such as skin rashes, urticaria, pruritus, sweating and facial oedema
Musculoskeletal, connective tissue and bone disorders	Frequency unknown	Uncontrolled muscle movements. Muscle rigidity
Renal and urinary disorders	Frequency unknown	Difficulty with micturition, urinary retention, ureteric spasm, dysuria, antidiuretic effect
Reproductive system and breast disorders	Frequency unknown	Sexual dysfunction, erectile dysfunction, decreased potency, decreased libido
General disorders and administrative site conditions	Frequency unknown	Malaise, tiredness, hypothermia

Reporting side effects

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of 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 Reactions Reporting Form", found online under SAHPRA's publications: hppts://www.sahpra.or.za/Publications/Index/8

HOTLINE for reporting of side effects directly to Innovata Pharmaceuticals (Pty) Ltd: 086 999 0912

4.9 Overdose

Triprolidine HCl

Overdosage with sedating antihistamines is associated with antimuscarinic, extrapyramidal, and CNS effects. When CNS stimulation predominates over CNS depression, which is more likely in children or the elderly, it causes ataxia, excitement, tremors, psychoses, hallucinations, and convulsions; hyperpyrexia may also occur. Coma and cardiorespiratory collapse may follow. In adults, CNS depression is more common with drowsiness, coma, and convulsions, progressing to respiratory failure and cardiovascular collapse.

Pseudoephedrine HCl

Symptoms

The symptoms of overdose include irritability, nervousness, tremor, cardiac dysrhythmias, palpitations, tachycardia, convulsions, urinary retention and hypertension, restlessness, dry mouth, anxiety, insomnia, nausea, vomiting and possible tolerance to pseudoephedrine as contained in **INNOSPECT**.

Treatment

Overdose should be treated by general supportive measures. Respiratory and circulatory
function should be maintained by supportive measures. Catheterisation of the bladder may be
required.

The benefit of gastric decontamination is uncertain. Consider activated charcoal (charcoal dose:
50 g for adults; 1 g/kg for children). Optimal effects are within 1 hour of ingestion of more than a
toxic dose. Monitor pulse, blood pressure and cardiac rhythm. Treat any hypertension or convulsions as necessary.

Guaiphenesin

(see section 4.8)

Treatment is symptomatic and supportive.

Codeine phosphate

Symptoms

Respiratory depression, pinpoint pupils, dry mouth, sweating and facial flushing are symptoms of overdose. High doses of codeine, as contained in **INNOSPECT**, may produce hypotension, circulatory failure, sedation, coma, or excitement and, in

children,

convulsions may occur.

Treatment

Treatment is symptomatic and supportive.

In acute overdosage with respiratory depression or coma, naloxone is indicated.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Opium derivatives and expectorants

ATC code: R05FA02

Mechanism of action

Triprolidine HCl

Triprolidine hydrochloride, an alkylamine derivative, is a sedating antihistamine with antimuscarinic and mild sedative effects.

Pseudoephedrine HCl

Pseudoephedrine is a direct and indirect acting sympathomimetic. It is a stereoisomer of ephedrine and has a similar action. Pseudoephedrine is given for the symptomatic relief of nasal congestion.

Guaiphenesin

Guaiphenesin is an expectorant that increases the volume and reduces the viscosity of tenacious sputum.

Codeine phosphate

Codeine phosphate, a phenanthrene derivative, is an opioid analgesic.

5.2 Pharmacokinetic properties

Triprolidine HCl

Absorption

After absorption from the gastrointestinal tract, triprolidine is metabolised to a carboxylated derivative which accounts for about half the dose excreted in the urine. Reported half-lives vary from 3 to 5 hours or more.

Pseudoephedrine HCl

Pseudoephedrine is well absorbed from the gastrointestinal tract. Pseudoephedrine HCl is excreted largely unchanged in the urine with small amounts of its hepatic metabolite.

Guaiphenesin

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

Codeine phosphate

Codeine is well absorbed from the gastrointestinal tract following oral administration. Codeine is metabolised in the liver to morphine and norcodeine which are both excreted in the urine partly as conjugates with glucuronic acid. The conversion of codeine to morphine is affected by the cytochrome P450 isoenzyme CYP2D6, which shows genetic polymorphism. Most of the excretion products appear in the urine within 6 hours and up to 86 % of the dose is excreted in 24 hours. About 70 % of the dose is excreted as free codeine, 10 % as free and conjugated morphine and a further 10 % as free or conjugated norcodeine. Only traces are found in the faeces. The plasma half-life is between approximately 3 and 4 hours.

6. Pharmaceutical excipients

6.1 List of excipients

Chloroform spirit:

- Chloroform
- Ethanol 96 %
- Purified water

Citric acid monohydrate, dye lennon yellow, flavour cola imitation, flavour peppermint, methylparaben, propylene glycol, purified water, sodium benzoate, sodium citrate, sodium cyclamate, sorbitol solution 70% (non-crystallising), sucrose.

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. Keep in original packaging until required for use.

6.5 Nature and contents of the container

Bottles of 100 and 200 ml.

7. Holder of certificate of registration

Innovata Pharmaceuticals

Crownwood Office Park

100 Northern Parkway

Ormonde

Johannesburg

8. REGISTRATION NUMBERS:

INNOSPECT PAEDIATRIC: Y/10.1/140

9. Date of first authorization/Renewal of the authorization

TBA

10. Date of revision of the text

09/12/2024