PROFESSIONAL INFORMATION

SCHEDULING STATUS: S3

1 NAME OF THE MEDICINE

PRESESE 5 mg TABLETS (tablet)

PRESESE 10 mg TABLETS (tablet)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

PRESESE 5 mg TABLETS: Each film-coated tablet contains bisoprolol fumarate (2:1)

5 mg. Sugar free.

PRESESE 10 mg TABLETS: Each film-coated tablet contains bisoprolol fumarate (2:1) 10 mg. Sugar free.

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

PRESESE 5 mg TABLETS:

Yellow coloured, circular, biconvex, film-coated tablets, debossed with ‘I and break line’ on one side and ‘11’ on the other side.

PRESESE 10 mg TABLETS:

Yellow coloured, circular, biconvex, film-coated tablets, debossed with ‘I and break line’ on one side and ‘13’ on the other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indication

PRESESE is indicated for the treatment of stable chronic moderate to severe heart failure with reduced systolic ventricular function (ejection fraction < 35 %, based on echocardiography), in addition to ACE inhibitors, and diuretics, and optionally digoxin, prior to the administration of **PRESESE.** The patients should have stable chronic heart failure without acute failure during the

previous six weeks and an unchanged basic therapy during the previous two weeks. They should be treated at optimal dose with an ACE inhibitor (or other vasodilator in case of intolerance to ACE inhibitors) and a diuretic, and optionally digoxin, prior to the administration of **PRESESE.** It is recommended that the treating medical practitioner should be experienced in the management of chronic heart failure.

4.2 Posology and method of administration

Posology

The treatment of stable chronic heart failure with **PRESESE** has to be initiated with a titration phase as given in the description below:

The treatment with **PRESESE** is to be started with a gradual up titration according to the following steps:

- 1.25 mg once daily for 1 week, if well tolerated increase to
- 2.5 mg once daily for a further week, if well tolerated increase to
- 3.75 mg once daily for a further week, if well tolerated increase to
- 5 mg once daily for the 4 following weeks, if well tolerated increase to
- 10 mg once daily for maintenance therapy.

After initiation of treatment with 1,25 mg, the patients should be observed over a period of approximately 4 hours (especially with regards to blood pressure, heart rate, conduction disturbances and signs of worsening of heart failure). The maximum recommended dose is 10 mg once daily.

Occurrence of adverse events may prevent all patients being treated with the maximum recommended dose. If necessary, the dose reached can also be decreased step by step. The treatment may be interrupted if necessary and reintroduced as appropriate. During the titration phase, in case of worsening of the heart failure or intolerance, it is recommended to first reduce the dose of **PRESESE**, or to stop immediately if necessary (in cases of severe hypotension, worsening of heart failure with acute pulmonary oedema, cardiogenic shock, symptomatic bradycardia or AV block).

Treatment of stable chronic heart failure with **PRESESE** is generally a long-term treatment. The treatment with **PRESESE** is not recommended to be stopped abruptly since this might lead to transitory worsening of heart failure. If discontinuation is necessary, the dose should be gradually decreased by dividing into halves, weekly.

There is wide interindividual variation in sensitivity to one single high dose of bisoprolol. Therefore, it is mandatory to initiate the treatment of these patients with a gradual up titration according to the scheme given.

Special populations

Elderly patients are more likely to have age-related peripheral vascular disease which may require caution.

Paediatric population

Safety and efficacy in children have not been established.

Method of administration

PRESESE should be taken in the morning and can be taken with food. They should be swallowed with liquid and should not be chewed.

4.3 Contraindications

PRESESE is contra-indicated in chronic heart failure patients with:

- hypersensitivity to bisoprolol or to any of the ingredients
- acute heart failure or during episodes of heart failure decompensation requiring IV inotropic therapy
- cardiogenic shock
- AV block of second or third degree (without a pacemaker)
- sick sinus syndrome
- sinoatrial block
- bradycardia with less than 50 beats/min before the start of therapy

- hypotension (systolic blood pressure less than 100 mmHg)
- bronchial asthma, bronchitis and severe chronic obstructive pulmonary disease
- peripheral arterial occlusive disease
- Raynaud's syndrome
- phaeochromocytoma
- metabolic acidosis
- pregnancy and lactation (see section 4.6)
- hyperthyroidism, as clinical manifestations may be masked
- peripheral vascular disease
- sinus bradycardia

4.4 Special warnings and precautions for use

PRESESE must be used with caution in:

- Concomitant treatment with inhalation anaesthetics
- diabetes mellitus with large fluctuations in blood glucose values; symptoms of hypoglycaemia can be masked, and responses to hypoglycaemia are diminished
- strict fasting

  PRESESE must be used with caution in fasting patients.
- ongoing desensitisation therapy
- AV block of first degree
- Prinzmetal's angina

  Beta-blockers, including **PRESESE**, may increase the number of chest pain attacks in patients who have Prinzmetal's angina.
- peripheral arterial occlusive disease (intensification of complaints might happen especially during the start of therapy). **PRESESE** may aggravate the symptoms of peripheral arterial occlusive disease (PAOD) or Raynaud's syndrome (due to unopposed arteriolar alpha-sympathetic activation). Severe peripheral vascular disease and even peripheral gangrene may be precipitated.

There is no therapeutic experience of **PRESESE** treatment in heart failure, in patients with the following diseases and conditions:

- NYHA class II heart failure
- insulin dependent diabetes mellitus (Type I)
- impaired renal function (serum creatinine <80 ml/min)
- impaired liver function
- patients older than 80 years
- restrictive cardiomyopathy
- congenital heart disease
- haemodynamically significant organic valvular disease
- myocardial infarction within 3 months

β- blockers, such as **PRESESE**, may cause bronchospasm in patients with asthma (see section 4.3). Bisoprolol may increase both the sensitivity towards allergens and the severity of anaphylactic reactions. Epinephrine (adrenaline) treatment does not always give the expected therapeutic effect.

Psoriasis may be aggravated by **PRESESE** and therefore must only be given **PRESESE** after careful consideration of the risks and benefits.
The symptoms of thyrotoxicosis may be masked under treatment with **PRESESE.**

Initiation of treatment with **PRESESE** necessitates regular monitoring. The cessation of therapy with **PRESESE** should not be done abruptly unless clearly indicated. Patients should be advised to limit the extent of their physical activity during the period in which **PRESESE** is being discontinued.
In patients undergoing general anaesthesia beta-blockade reduces the incidence of arrhythmias and myocardial ischaemia during induction and intubation, and the postoperative period. The anaesthetist must be aware of beta-blockade because of the potential for interactions with other medicines, resulting in bradydysrhythmias, attenuation of the reflex tachycardia and the decreased reflex ability to compensate for blood loss.
A patient's normal tachycardiac response to hypovolaemia or blood loss may be obscured during or after surgery. Particular caution should be taken in this regard. In the event of surgery, the anaesthetist should be informed of therapy with **PRESESE** prior to any operation. If the decision is made to withdraw **PRESESE** before anaesthesia, at least 48 hours should be allowed to elapse between the last dose and surgery. If the medicine is to be continued, care should be taken when

using halogenated anaesthetics. Atropine (1 – 2 mg IV) may be used to correct vagal dominance. The patient must be maintained on their usual dosage peri-operatively. In the peri-operative period it is generally unwise to reduce the dosage to which the patient is accustomed, as there may be danger of aggravation of angina pectoris or hypertension.

In patients suffering from ischaemic heart disease, treatment should not be discontinued abruptly. The dosage of **PRESESE** should be adjusted in severe renal impairment.

Care should be taken in prescribing **PRESESE** together with Class 1 antidysrhythmic medicines such as disopyramide, myocardial depressants and inhibitors of AV conduction such as calcium antagonists. Caution should be exercised when transferring a patient from clonidine, as the withdrawal of clonidine may result in the release of large amounts of catecholamines that may give rise to a hypertensive crisis. If **PRESESE** is administered in these circumstances, the unopposed alpha receptor stimulation may potentiate this effect.

If **PRESESE** and clonidine are given concurrently the clonidine should not be discontinued until several days after the withdrawal of **PRESESE**, as severe rebound hypertension may occur.

PRESESE should be used with caution in combination with verapamil in patients with impaired ventricular function. This combination should not be given to patients with conduction abnormalities. Neither medicine should be administered intravenously within 48 hours of discontinuing the other. The intravenous administration of calcium antagonists and antidysrhythmic medicines is not recommended during therapy with **PRESESE.** The intravenous administration of verapamil in patients on treatment with **PRESESE** may lead to profound hypotension and atrioventricular block.
PRESESE modifies the tachycardia associated with hypoglycaemia.

Patients with phaeochromocytoma usually require treatment with an alpha-adrenergic blocker.
PRESESE may increase both the sensitivity towards allergens and the severity of anaphylactic reactions. Adrenaline treatment does not always give the expected therapeutic effect. **PRESESE** may mask the symptoms of hyperthyroidism.

The normal dose should be reduced in elderly patients, or in patients suffering from renal dysfunction. A patient's normal tachycardiac response to hypovolaemia or blood loss may be obscured during or after surgery. Particular caution should be taken in this regard.

Cases of coronary vasospasm have been observed. Despite its high $beta_1$-selectivity, angina attacks cannot be completely excluded when **PRESESE**, is administered to patients with Prinzmetal's angina. Utmost caution must be exercised.

Treatment with **PRESESE** must not be withdrawn abruptly unless clearly indicated (see section 4.2).
Abrupt discontinuation of therapy with **PRESESE** may cause exacerbation of angina pectoris in patients suffering from ischaemic heart disease, myocardial infarction, ventricular dysrhythmias and in some cases could lead to sudden death.
Discontinuation of **PRESESE** should be gradual over a period of 1 to 2 weeks, and patients should be advised to limit the extent of their physical activity during the period that **PRESESE** is being discontinued.

Caution is warranted when treating patients with hypertension or angina pectoris and concomitant heart failure with **PRESESE**.

Digitalisation of patients receiving long-term beta-blocker therapy including **PRESESE** may be necessary if congestive cardiac failure is likely to develop. This combination can be considered despite the potentiation of the negative chronotropic effect of the two medicines. Careful control of dosages, and of the individual patient's response (and notably pulse rate), is essential in this situation.

Beta-blockers, including **PRESESE**, may unmask myasthenia gravis.
Although cardioselective (beta1) beta-blockers may have less effect on lung function than nonselective beta-blockers, these should be avoided in patients with obstructive airways diseases, unless there are compelling clinical reasons for their use. Where such reasons exist, **PRESESE** may

be used with caution. In bronchial asthma or other chronic obstructive pulmonary diseases, which may cause symptoms, concomitant bronchodilating therapy is recommended. Occasionally an increase of the airway resistance may occur in patients with asthma, therefore, the dose of beta$_2$-stimulants may have to be increased.

Paediatric population

Safety and efficacy in children have not been established.

4.5 Interaction with other medicines and other forms of interaction

It can be dangerous to administer **PRESESE** with the following medicines:

- Concomitant use of **PRESESE** with hypoglycaemic medicines, phenothiazines and various antidysrhythmic medicines can have life-threatening consequences, e.g.
    - profound hypoglycaemia with oral hypoglycaemic medicines and insulin;
    - myocardial depression with antidysrhythmic medicines.
- Beta-adrenoceptor stimulating medicines (e.g. isoprenaline, dobutamine) may antagonise the effects of **PRESESE.** Combination with **PRESESE** may reduce the effect of both medicines. Higher doses of epinephrine (adrenaline) may be necessary for treatment of allergic reactions.
- Sympathomimetics that activate both beta- and alpha-adrenoceptors (e.g. norepinephrine(noradrenaline), epinephrine (adrenaline)): Combination with **PRESESE** may unmask the alpha-adrenoceptor-mediated vasoconstrictor effect of these medicines leading to blood pressure increase and exacerbated intermittent claudication.
- Alpha-adrenoceptor stimulants can dangerously affect the vasoconstrictor effects and adrenergic neuron blocking medicines may lead to life-threatening vasoconstriction when used in combination with **PRESESE.**
- **PRESESE** and digoxin may be used concomitantly for patients with congestive heart failure provided that the pulse rate and patient response is monitored.

  It can be dangerous to administer **PRESESE** with digoxin which can lead to a reduction of heart rate and an increase of atrio-ventricular conduction time.

- Dihydropyridine-type calcium antagonists such as nifedipine and amlodipine, should not be used in combination with **PRESESE** since this may increase the risk of hypotension. In patients with heart failure, an increase in the risk of further deterioration of the ventricular pump function cannot be excluded.
- Atrio-ventricular conduction time, as well as negative inotropic effect, may be increased when **PRESESE** is used concurrently with Class-I antidysrhythmic medicines (e.g. disopyramide and quinidine, lidocaine, phenytoin, flecainide, propafenone). Atrioventricular conduction time may also be increased when **PRESESE** is taken concomitantly with Class-III antidysrhythmic medicines (e.g. amiodarone). The half-life of **PRESESE** can be slightly shortened by the simultaneous administration of rifampicin. An increase in the dose is generally unnecessary.
- Calcium antagonists, such as verapamil, and to a lesser degree diltiazem, have a negative influence on contractility, atrio-ventricular conduction and blood pressure (see section 4.4). In patients on **PRESESE**, the I.V. administration of verapamil may cause profound atrioventricular block and hypotension. The use of **PRESESE** in combination with calcium antagonists is therefore not recommended.
- Clonidine and other centrally acting antihypertensives medicines such as methyldopa, moxonodine and rilmenidine may further decrease heart rate, cardiac output and vasodilation if taken together with **PRESESE**.

  Beta-blockers, such as **PRESESE** may exacerbate the “rebound hypertension” which can occur in case of abrupt withdrawal of centrally acting antihypertensive medicines (e.g. Clonidine). If the two medicines are co-administered, the β-blocker should be withdrawn several days before discontinuing clonidine. If replacing clonidine by β-blocker therapy, the introduction of β-blockers should be delayed for several days after clonidine administration has stopped.
- Mono amine oxidase inhibitors (except MAO-B inhibitors) enhance the hypotensive effect of β-blockers as well as the risk of hypertensive crisis.
- The pharmacokinetics of bisoprolol is not significantly influenced by cimetidine.
- The following combinations should be used with caution together with bisoprolol:
  - Class-I antidysrhythmic medicines (e.g. disopyramide, quinidine), due to a potentiated effect on the atrial conduction time and an increased negative inotropic effect.

  - Class-III antidysrhythmic medicines (e.g. amiodarone), where the effect an atrial conduction time may be potentiated.

- Parasympathomimetic medicines (including tacrine), where atrio-ventricular conduction time and risk of bradycardia may be increased.
- Other β-blockers, including eye drops, have additive effects.
- Insulin and oral antidiabetic medicines, where it can lead to an intensification of the blood sugar lowering effect. Blockade of β-adrenoceptors may mask symptoms of hypoglycaemia.
- Anaesthetic medicines which can lead to attenuation of reflex tachycardia and increase the risk of hypotension. Continuation of β-blockade reduces the risk of dysrhythmia during induction and intubation. The anaesthetist should be informed when the patient is receiving **PRESESE.**
- Prostaglandin synthetase inhibiting medicines, where the hypotensive effect is decreased.
- Ergotamine derivatives which can lead to an exacerbation of peripheral circulatory disturbances.
- Combinations of sympathomimetic medicines with **PRESESE** may reduce the effect of both medicines. Higher doses of epinephrine (adrenaline) may be necessary for treatment of allergic reactions.
- **PRESESE** in combination with tricyclic antidepressants, barbiturates, phenothiazines, as well as other antihypertensive medicines, can lead to an increased blood pressure lowering effect.
- The combination of **PRESESE** with mefloquine should be considered, as there is an increased risk of bradycardia.

4.6 Fertility, pregnancy and lactation

Pregnancy

The use of **PRESESE** during pregnancy is not recommended (see section 4.3).

PRESESE has pharmacological effects that may cause harmful effects on pregnancy and/or the foetus/newborn. **PRESESE** reduce placental perfusion, which has been associated with growth retardation, intrauterine death, abortion or early labour.

Administration of **PRESESE** to pregnant mothers shortly before birth or during labour may result in hypotonia, collapse or hypoglycaemia in the newborn. (See section 4.3).

Breastfeeding

It is not known whether **PRESESE** passes into breast milk.

Therefore, breastfeeding is not recommended during treatment with **PRESESE.**

Fertility

No effect on fertility was observed in male or female rats treated with bisoprolol at oral doses up to 150 mg/kg/day.

4.7 Effects on ability to drive and use machines

PRESESE may cause drowsiness and dizziness. Do not drive or use any tools or machines until you know how the tablets affect you.

4.8 Undesirable effects

a) Summary of the safety profile

Adverse reactions are more common in patients with renal decompensation.

b) Tabulated list of adverse reactions

- Frequency unknown- cannot be estimated from the available data.

System Organ Class	Adverse effect	Frequency
Blood and the lymphatic system disorders	Leukopenia, thrombocytopenia, agranulocytosis, non-thrombocytopenia purpura, transient eosinophilia	*Less frequent:*
Immune system disorders	Hypersensitivity reactions (itching, flush, rash), systemic lupus erythematosus (SLE)	*Less frequent*
Metabolism and nutrition disorders	Metabolic disturbances	*Less frequent*

	Hypoglycaemia, hyperglycaemia, increase in uric acid levels, hypercholesterolaemia Increased triglycerides, increased liver enzymes (ALAT, ASAT).	*Frequency unknown*
Psychiatric disorders	Sleep disturbances, depression, nightmares, hallucinations, overt psychosis, amnesia, anxiety, nervousness, sleep disorders or trouble sleeping, nightmares and vivid dreams, hallucinations, confusion.	*Less frequent*
	Restlessness	*Frequency unknown*
Nervous system disorders	Lassitude, fatigue, dizziness, mild headache, unusual tiredness/weakness, exhaustion, headache (these symptoms generally occur at the beginning of treatment),	*Frequent*
	Sleep disorders, coma, convulsions	*Less frequent*
Eye disorders	Conjunctivitis, decreased tear production, blurred vision, soreness, disturbances of vision	*Less frequent*
	Disturbances of vision	*Frequency unknown*
Ear and labyrinth disorders	Transient hearing loss, hearing impairment	*Less frequent*
Cardiac disorders	Bradycardia, heart block, fluid retention, syncope, congestive cardiac failure, AV-stimulus disturbances, worsening of heart failure.	*Less frequent*
Vascular disorders	Cold extremities, hypotension, paraesthesia, feeling of coldness and numbness in the extremities	*Frequent*

	Paradoxical hypertension, exacerbation of peripheral vascular disease or the development of Raynaud's phenomenon, restlessness, severe peripheral vascular disease and peripheral gangrene, orthostatic hypertension.	*Less frequent*
Respiratory, thoracic and mediastinal disorders	Bronchospasm in patients with bronchial asthma or history of obstructive airways disease, shortness of breath, dyspnea, pneumonia, pulmonary fibrosis, pleurisy	*Less frequent*
Gastrointestinal disorders	Nausea, vomiting, diarrhoea, constipation, abdominal cramping and other gastro-intestinal disturbances	*Frequent*
	Stomatitis	*Frequency unknown*
Hepatobiliary disorders	Hepatotoxicity, hepatitis	*Less frequent*
Skin and subcutaneous tissue disorders	Perspiration	*Frequent*
	*S*kin rash, allergic reactions	*Less frequent*
	Alopecia, rash, pruritus, exacerbation of psoriasis	*Frequency unknown*
Musculoskeletal, connective tissue and bone disorders	Muscle weakness, cramps, myopathies, back and joint pain	*Less frequent*
Reproductive system and breast disorders	Decreased sexual ability	*Frequent*
	Potency disorders, impotence	*Less frequent*
General disorders and administrative conditions	Fatigue*, lassitude	*Frequent*
	Mass gain, asthenia	*Less frequent*
	Sclerosing peritonitis, retroperitoneal fibrosis.	*Frequency unknown*

*This symptom especially occurs at the beginning of therapy. It is generally mild and often disappears within 1 – 2 weeks.

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 requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

4.9 Overdose

Overdosage may produce bradycardia and severe hypotension. Bronchospasm and heart failure may be produced in certain individuals as well as acute cardiac insufficiency, cardiac conduction block, heart failure, cardiogenic shock and hypoglycaemia.

Coma and convulsions have also been reported, and some patients may develop severe and occasionally fatal cardiovascular depression. Cases of overdose should be observed for at least 4 hours, as apnoea and cardiovascular collapse may appear suddenly.

Treatment

Generally, in cases of overdose, the patient should stop taking **PRESESE** and supportive and symptomatic treatment should be provided.

Repeated activated charcoal is necessary in severe overdose

The data available suggest that bisoprolol is not dialysable to any extent.

Atropine may be administered intravenously to treat severe bradycardia. If the response is inadequate, isoprenaline or another medicine with positive chronotropic properties may be given cautiously. Under some circumstances, transvenous pacemaker insertion may be necessary

Alternatively, dobutamine may be required to reverse beta-blockade. Cardiac pacing may be required for severe bradycardia.

Hypotension: Vasopressors and I.V. fluids should be administered.

Glucagon may be given intravenously, with sympathomimetics used as an alternative or given with glucagon.

AV block (second or third degree): Monitor patients closely and treat with isoprenaline infusion or insert a cardiac pacemaker.

Acute worsening of heart failure: Recommended treatment includes I.V. diuretics, inotropic medicines and vasodilating medicines.

Bronchospasm should be treated with bronchodilator therapy such as isoprenaline, β2-sympathomimetic medicines and/or aminophylline. Beta-agonist (e.g. salbutamol) or xanthines may also be given.

Hypoglycaemia: I.V. glucose or glucagon can be administered.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacological classification: A 5.2 Adrenolytics (sympathicolytics).

Pharmacotherapeutic group: Beta blocking agents, selective

ATC Code: C07AB07

Bisoprolol is a selective β_1-adrenoceptor antagonist with low β_2 receptor affinity. It is devoid of intrinsic sympathomimetic and membrane-stabilising activity.

It reduces blood pressure, and by blockade of the cardiac β_1-receptors, it reduces cardiac action, and hence myocardial oxygen demand.

5.2 Pharmacokinetic properties

Absorption

Bisoprolol is well absorbed following oral administration with a resultant bioavailability of about 90 %, T_{max} is at 3 hours.

The plasma protein binding of bisoprolol is about 30 %. The distribution volume is 3.5 l/kg. The total clearance is approximately 15 l/h. The kinetics of bisoprolol are linear.

Distribution

The plasma elimination half-life is approximately 10 to 12 hours in healthy volunteers and the duration of action is about 24 hours.

Biotransformation and Elimination

About 50 % of a dose is metabolised in the liver and the remainder is excreted unchanged via the kidneys. Since the elimination takes place in the kidneys and the liver to the same extent a dosage adjustment is not required for patients with impaired liver function or renal insufficiency

Special populations

In patients with chronic heart failure, patients with renal impairment and in patients with liver cirrhosis, the plasma levels of bisoprolol are about one third higher and the half-life is prolonged. In the elderly with hypertension, the elimination is delayed, and plasma levels are higher.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Calcium hydrogen phosphate
- Cellulose microcrystalline
- Crospovidone
- Magnesium stearate
- Silica colloidal anhydrous

The coating material of **PRESESE** contains:

- Hypromellose
- Macrogol / peg 400
- Titanium dioxide (c.i. no: 77891)
- Purified water
- Iron oxide yellow

6.2 incompatibilities

Not applicable.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at or below 25 °C. Protect from light and moisture.

Keep blisters in the original carton until required for use.

Keep the containers tightly closed.

6.5 Nature and contents of container

PRESESE 5 mg TABLETS AND PRESESE 10 mg TABLETS:

Blister pack:

Tablets are packed in printed peelable lidding silver foil (50 g/m^2 paper / 12 micron polyster / 20 micron Aluminium foil / 7 g/m^2 HSL) and cold form film (25 micron polyamide / 45 micron Aluminium foil / 60 micron PVC film). One blister contains 10 tablets.

Pack size: 30's: Each carton contains 3 blisters of 10 tablets each.

HDPE Container Pack:

Tablets are packed in white opaque round 40 ml HDPE container with a white opaque ribbed stock (RS) HDPE closure, with induction sealing wad containing one silica gel sachet. Each container which is enclosed in an outer cardboard carton contains 30 tablets.

Pack size: 30's - One HDPE container contains 30 tablets.

6.6 Special precautions for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION

Aurogen South Africa (Pty) Ltd

Woodhill Office Park, Building 1, First floor,

53 Phillip Engelbrecht Avenue

Meyersdal, Ext. 12, 1448

Johannesburg

South Africa

8 REGISTRATION NUMBER(S)

PRESESE 5 mg TABLETS: 45/5.2/0866

PRESESE 10 mg TABLETS: 45/5.2/0867

9 DATE OF FIRST AUTHORISATION/ RENEWAL OF THE AUTHORISATION

11 June 2018

10 DATE OF REVISION OF THE TEXT

19 December 2024