SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

Phenylephrine 50 µg/mL PS Equity solution for injection in prefilled syringe.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each mL of the solution contains phenylephrine hydrochloride equivalent to 50 micrograms (0,05 mg) of phenylephrine.

Each 10 mL pre-filled syringe contains phenylephrine hydrochloride equivalent to 500 micrograms (0,5 mg) of phenylephrine.

Excipient(s) with known effect:

Each ml of solution for injection contains 3,72 mg equivalent to 0,162 mmol of sodium.

Each 10 ml pre-filled syringe contains 37,2 mg equivalent to 1,62 mmol of sodium.

Phenylephrine 50 µg/mL PS Equity is sugar free.

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection in pre-filled syringe.

A clear, colourless, pyrogen free and sterile solution for injection.

pH 4,7 – 5,3

2025.06.17

Osmolarity: 270 – 300 mOsm/kg.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Phenylephrine 50 µg/mL PS Equity is indicated for the treatment of hypotension during spinal, epidural or general anaesthesia.

4.2 Posology and method of administration

Posology

Adults

Normal dose is 50 to 100 micrograms, which can be repeated until the desired effect is obtained. One bolus dose should not exceed 100 micrograms.

Special population

Patients with renal impairment

Lower doses of Phenylephrine 50 µg/mL PS Equity may be required in patients with impaired renal function.

Patients with hepatic impairment

Higher doses of Phenylephrine 50 µg/mL PS Equity L may be needed in patients with cirrhosis of the liver.

Elderly patients

Treatment of the elderly should be carried out with care.

Paediatric population

The safety and efficacy of Phenylephrine 50 µg/mL PS Equity in children have not been established. No

2025.06.17

data are available.

Method of administration

Intravenous bolus injection.

Phenylephrine 50 µg/mL PS Equity should only be administered by healthcare professionals with appropriate training and relevant experience.

The pre-filled syringe is not suitable for use in a syringe driver.

4.3 Contraindications

- Hypersensitivity to phenylephrine hydrochloride or to any of the excipients listed in section 6.1.
- Patients with severe hypertension.
- Patients with peripheral vascular disease, as it can lead to ischaemia with a risk of gangrene or vascular thrombosis.
- Patients with heart-block with or without bradycardia, uncontrolled cardiac failure, bradycardia less than 50 bpm or seriously impaired coronary arterial circulation.
- In combination with indirectly acting sympathomimetic medicines (ephedrine, methylphenidate, pseudoephedrine): risk of vasoconstriction and/or hypertensive crisis.
- In combination with alpha-sympathomimetic medicines (oral and/or nasal use) (etilefrine, midodrine, naphazoline, oxymetazoline, synephrine, tetryzoline, tuaminoheptane, tymazoline): risk of vasoconstriction and/or hypertensive crisis.
- In combination with non-selective monoamine oxidase inhibitors (MAOs) (or within 2 weeks of their withdrawal), due to risk of paroxysmal arterial hypertension and possibly fatal hyperthermia (see section 4.5).
- Patients with severe hyperthyroidism.

2025.06.17

4.4 Special warnings and precautions for use

Arterial blood pressure should be monitored during treatment.

Phenylephrine 50 µg/mL PS Equity should be given with caution to patients with:

- diabetes mellitus
- arterial hypertension
- aneurysm
- uncontrolled hyperthyroidism
- coronary heart disease and chronic heart conditions
- non-severe peripheral vascular insufficiency
- bradycardia
- partial heart block
- tachycardia
- dysrhythmias
- angina pectoris (phenylephrine can precipitate or exacerbate angina in patients with coronary artery disease and history of angina)
- peripheral vascular diseases e.g. Raynaud's phenomenon
- closed angle glaucoma.

Phenylephrine 50 µg/mL PS Equity can induce a reduction in cardiac output. Therefore, care should be exercised in administering to patients with arteriosclerosis, the elderly and to patients with impaired cerebral or coronary circulation.

In patients with reduced cardiac output or peripheral or coronary vascular disease, vital organ functions should be closely monitored and dose reduction should be considered when systemic blood pressure is near the lower end of the target range.

2025.06.17

In patients with serious heart failure or cardiogenic shock, Phenylephrine 50 µg/mL PS Equity may cause deterioration in the heart failure as a consequence of the induced vasoconstriction (increase in afterload).

Particular attention should be paid when administering Phenylephrine 50 µg/mL PS Equity injection to avoid extravasation, since this may cause tissue necrosis.

Lower doses may be required in patients with renal impairment (see section 4.2).
Higher doses may be required in patients with liver cirrhosis (see section 4.2).

Allergic reactions, including anaphylactic shock, may occur in patients with sulphite-sensitivity.

Blood pressure response to Phenylephrine 50 µg/mL PS Equity may be increased in patients with autonomic dysfunction.

The administration of Phenylephrine 50 µg/mL PS Equity simultaneously with the following medicines is not recommended, because of the risk of vasoconstriction and/or hypertensive crisis associated with its indirect sympathomimetic effect (see section 4.5):

- dopaminergic ergot alkaloids (bromocriptine, carbergoline, lisuride or pergolide) or vasoconstrictors (dihydroergotamine, ergotamine, or methysergide, methylergometrine).
- in combination with linezolid.

Concurrent use with MAO inhibitors may prolong and intensify cardiac stimulation and vasopressor effects because of the release of catecholamines, which accumulate in intraneuronal storage sites during MAO inhibitor therapy; this may result in headache, cardiac dysrhythmias, vomiting or sudden and severe hypertensive or hyper-pyretic crises.

2025.06.17

For patients who have been receiving MAO inhibitors 2 to 3 weeks prior to administration of sympathomimetic medicines, the initial dosage should be reduced to be no more than one-tenth of the usual dose (see section 4.5).

This medicine contains 37,2 mg sodium per pre-filled syringe, equivalent to 1,9 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.

4.5 Interaction with other medicines and other forms of interaction

Contraindicated combinations (see section 4.3)

- *Non-selective monoamine oxidase inhibitors (MAOs) (iproniazid, nialamide, phenelzine)*

Increased risk of paroxysmal hypertension, hyperthermia possibly fatal. Due to the long duration of action of MAOIs, this interaction is still possible 15 days after discontinuation of the MAOI.

- *Indirect sympathomimetics medicines (ephedrine, methylphenidate, pseudoephedrine):*

Increased risk of vasoconstriction and / or hypertensive crisis.

- *Alpha sympathomimetic medicines (oral and/or nasal use) (etilefrine, midodrine, naphazoline, oxymetazoline, synephrine, tetryzoline, tuaminoheptane, tymazoline):*

Increased risk of vasoconstriction and / or hypertensive crisis.

Combinations not recommended (see section 4.4)

- *Dopaminergic ergot alkaloids (bromocriptine, cabergoline, lisuride, pergolide):*

Increased risk of vasoconstriction and/or hypertensive crisis.

- *Vasoconstrictor ergot alkaloids (dihydroergotamine, ergotamine, methylergometrine, methylsergide):*

Increased risk of vasoconstriction and/or hypertensive crisis.

2025.06.17

- *Tricyclic antidepressants (desipramine, imipramine, nortriptyline):*

Increased risk of paroxysmal hypertension with possibility of dysrhythmias (inhibition of adrenaline or noradrenaline entry in sympathetic fibres).

- *Noradrenergic-serotoninergic antidepressants (minalcipram, venlafaxine):*

Increased risk of paroxysmal arterial hypertension with possibility of dysrhythmias (inhibition of adrenaline or noradrenaline entry in sympathetic fibres).

- *Selective type A monoamine oxidase inhibitors (MAOs) (moclobemide, pargyline, selegiline, toloxatone):*

Increased risk of vasoconstriction and/or hypertensive crisis.

- *Linezolid:*

Increased risk of vasoconstriction and/or hypertensive crisis.

- *Guanethidine and related products:*

Substantial increase in blood pressure (hyperreactivity linked to the reduction in sympathetic tone and/or to the inhibition of adrenaline or noradrenaline entry in sympathetic fibres). If the combination cannot be avoided, use with caution lower doses of sympathomimetic medicines.

- *Cardiac glycosides, quinidine:*

Increased risk of dysrhythmias.

- *Sibutramine:*

Paroxysmal hypertension with possibility of dysrhythmias (inhibition of adrenaline or noradrenaline entry

2025.06.17

in sympathetic fibres).

- *Halogenated volatile anaesthetics (desflurane, enflurane, halothane, isoflurane, methoxyflurane, sevoflurane):*

Risk of perioperative hypertensive crisis and dysrhythmia.

The effect of antihypertensive and diuretic medicines used as antihypertensives may be reduced when used concurrently with Phenylephrine 50 µg/mL PS Equity; the patient should be carefully monitored to confirm the desired effect is obtained.

Beta-adrenoceptor-blocking medicines, systemic or ophthalmic - concurrent use of Phenylephrine 50 µg/mL PS Equity may result in an exaggeration of the vasoconstriction effects and profound bradycardia.

Reserpine and other sympatholytic medicines - concomitant use with Phenylephrine 50 µg/mL PS Equity causes a substantial increase in blood pressure. If the combination cannot be avoided, use with caution.

The pressor effect of Phenylephrine 50 µg/mL PS Equity is increased in patients receiving atropine sulphate.

Combinations requiring precautions for use:

- *Oxytocic medicines:*

The effect of pressor-active sympathomimetic amines is potentiated. Thus, some oxytocic medicines may cause severe persistent hypertension and strokes can occur during post-partum period.

Digoxin: Phenylephrine 50 µg/mL PS Equity may be used with digoxin for therapeutic advantage; caution

2025.06.17

and close electrocardiographic monitoring are recommended during concurrent use.

Alpha-adrenoceptor-blocking medicines (doxazosin, labetalol, prazosin, haloperidol, phenothiazines): concurrent use may antagonise the peripheral vasoconstriction effect of Phenylephrine 50 µg/mL PS Equity.

4.6 Fertility, pregnancy and lactation

Pregnancy

The safety of Phenylephrine 50 µg/mL PS Equity during pregnancy has not been established.

Animal studies are insufficient with respect to effects on pregnancy, embryonal / foetal development, parturition or postnatal development. The potential risk for humans is unknown.
Phenylephrine 50 µg/mL PS Equity may be used for the treatment of hypotension during pregnancy.

The combination with some oxytocic medicines can cause severe hypertension (see section 4.5).

Breastfeeding

The safety of Phenylephrine 50 µg/mL PS Equity during breastfeeding has not been established.

Small amounts of phenylephrine are excreted in human milk. The administration of vasoconstrictors to the mother puts the child at risk for cardiovascular and neurological effects. Phenylephrine 50 µg/mL PS Equity should not be used during lactation. However, in the event of a single bolus administration during childbirth, breastfeeding is possible.

Fertility

There are no data available regarding human fertility, following treatment with

2025.06.17

Phenylephrine 50 µg/mL PS Equity.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

a. Summary of the safety profile

The most frequent adverse events of Phenylephrine 50 µg/mL PS Equity are bradycardia, hypertensive episodes, nausea and vomiting. Hypertension is more frequent with high doses.

The most frequently reported cardiovascular adverse event appears to be bradycardia, likely due to baroreceptor-mediated vagal stimulation and consistent with the pharmacological effect of phenylephrine.

b. Tabulated list of adverse reactions

Immune system disorders	
Less frequent	Hypersensitivity
Metabolism and nutrition disorders	
*Frequency unknown**	Abnormal glucose metabolism
Psychiatric disorders	
Less frequent	Anxiety, excitability, agitation, psychotic states, confusion
Nervous system disorders	
Frequent	Headache
Less frequent	Tingling, fullness head, nervousness or restlessness, insomnia, paraesthesia, tremor
Eye disorders	

2025.06.17

Less frequent	Mydriasis, aggravation of pre-existing angle-closure glaucoma
Cardiac disorders	
Less frequent	Anginal pain, reflex bradycardia, tachycardia, ventricular dysrhythmias
*Frequency unknown**	Dysrhythmia, cardiac arrest, palpitations, myocardial ischemia, angina pectoris
Vascular disorders	
Less frequent	Cerebral haemorrhage, hypertension, hypotension with dizziness, hypertensive crisis, pallor
*Frequency unknown**	Fainting, flushing, coldness of skin
Respiratory, thoracic and mediastinal disorders	
Less frequent	Dyspnoea, pulmonary oedema
Gastrointestinal disorders	
Less frequent	Nausea, vomiting
*Frequency unknown**	Hypersalivation
Skin and subcutaneous system disorders	
Less frequent	Piloerection, sweating, skin blanching
*Frequency unknown**	Diaphoresis
Musculoskeletal and connective tissue disorders	
Less frequent	Muscular weakness
Renal and urinary disorders	
Less frequent	Difficulty in micturition, urinary retention
General disorders and administration site conditions	
Less frequent	Extravasation necrosis at injection site

2025.06.17

* Frequency cannot be estimated from available data.

c. Description of selected adverse reactions

As Phenylephrine 50 µg/mL PS Equity has been frequently used in the critical care setting in patients with hypotension and shock, some of the reported serious adverse events and deaths are probably related to the underlying disease and not related to the use of phenylephrine (e.g., Phenylephrine 50 µg/mL PS Equity).

d. Other special population(s)

Elderly: risk for phenylephrine toxicity is increased in elderly patients (see section 4.4).

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

4.9 Overdose

Symptoms

Symptoms of overdose include headache, nausea, vomiting, paranoid psychosis, hallucinations, hypertension and reflex bradycardia. Cardiac dysrhythmia such as ventricular extrasystoles and short paroxysmal episodes of ventricular tachycardia may occur.

Treatment

Treatment should consist of symptomatic and supportive measures. The hypertensive effects may be treated with an appropriate antihypertensive medicine e.g. magnesium sulfate.

2025.06.17

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacological classification: 6.1 Cardiac stimulants

Pharmacotherapeutic group: Cardiac stimulants, excluding cardiac glycosides

ATC code: C01C A06

Mechanism of action

Phenylephrine acts predominantly by direct stimulation of alpha1-adrenergic receptors. In therapeutic doses, it has no substantial stimulant effect on the beta-adrenergic receptors of the heart (beta1-adrenergic receptors), but substantial activation of these receptors may occur when larger doses are given. Phenylephrine does not stimulate beta-adrenergic receptors of the bronchi or peripheral blood vessels (beta2-adrenergic receptors). It is believed that alpha1-adrenergic effects result from the inhibition of the production of cyclic adenosine-3',5'-monophosphate (cAMP) by inhibition of the enzyme adenyl cyclase, whereas beta-adrenergic effects result from stimulation of adenyl cyclase activity. Phenylephrine also has an indirect effect by releasing norepinephrine from its storage sites.

Pharmacodynamic effects

The predominant actions of phenylephrine are on the cardiovascular system. Parenteral administration causes a rise in systolic and diastolic pressures. Accompanying the pressor response to phenylephrine is a marked reflex bradycardia that can be blocked by atropine; after atropine, large doses of the medicine increase the heart rate only slightly. Cardiac output is slightly decreased and peripheral resistance is considerably increased. Circulation time is slightly prolonged, and venous pressure is slightly increased; venous constriction is not marked. Most vascular beds are constricted; renal splanchnic, cutaneous and limb blood flows are reduced but coronary blood flow is increased. Pulmonary vessels are constricted, and pulmonary arterial pressure is raised.

2025.06.17

Clinical efficacy and safety

Phenylephrine is a potent vasoconstrictor that acts almost exclusively through stimulation of alpha-1-adrenergic receptors. Such arterial vasoconstriction, also accompanied by venous vasoconstriction, provides an increase in blood pressure and bradycardia reflex and its pressor activity is weaker than that of noradrenaline but of longer duration. It is used parenterally in the treatment of hypotensive states, such as those encountered during circulatory failure, general or spinal anaesthesia or medicine induced hypotension. In many published clinical studies phenylephrine was used in low-risk pregnant women undergoing spinal anaesthesia during Caesarean delivery.

Phenylephrine allowed maintenance of maternal blood pressure near to baseline and reduced the incidence of nausea and vomiting without causing foetal acidosis.

In therapeutic doses, phenylephrine produces little if any stimulation of either the spinal cord or cerebrum. Repeated injections of phenylephrine do not produce tachyphylaxis, although this can occur with prolonged infusion.

The potent arterial vasoconstriction results in an increase in afterload and may result in reduced ventricular ejection fraction. This may result in a reduction of cardiac output, that is less pronounced in healthy people but can be exacerbated in the case of previous heart failure.

5.2 Pharmacokinetic properties

Absorption

After intravenous (IV) administration, a pressor effect occurs almost immediately and persists for 15 – 20 minutes.

Distribution

2025.06.17

Phenylephrine undergoes rapid distribution into peripheral tissues; there is some evidence that it may be stored in certain organ compartments. Plasma protein binding is unknown. The volume of distribution is 340 litres, after a single dose, exceeded the body volume by a factor of 5, suggesting a high distribution into certain organ compartments. The pharmacologic effects of phenylephrine are terminated at least partially by uptake into tissues. Penetration of phenylephrine into the central nervous system (CNS) appears to be minimal. Phenylephrine does not appear to be distributed to any great extent into breast milk. The average total serum clearance (2 095 mL/min) was close to one-third of the cardiac output.

Biotransformation

Phenylephrine is metabolized in the liver by mono amine oxidase (MAO).

Elimination

The elimination of phenylephrine is primarily urinary and elimination via the renal route seems to be similar between the IV and per oral routes; 86 % and 80 % of the administered dose, respectively. The short duration of action of phenylephrine (about 20 minutes after IV injection) suggests a rapid distribution, metabolism and elimination from the body.

Special Populations

There are no data available on the pharmacokinetics in special populations.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Citric Acid monohydrate

Sodium citrate

Sodium chloride

Sodium hydroxide (pH adjuster)

2025.06.17

Water for injection

6.2 Incompatibilities

In the absence of compatibility studies, this medicine must not be mixed with other medicines.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store at or below 30 °C.

Store the syringe in the unopened blister until use. Keep the blister in the outer carton in order to protect from light.

6.5 Nature and contents of container

Phenylephrine 50 µg/mL PS Equity is presented in a sterile 10 ml polypropylene pre-filled syringe, ready-to-use, packaged in a unitary transparent blister pack.

The pre-filled syringes are available in box of 10 syringes.

6.6 Special precautions for disposal and other handling

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

Instructions for use:

Please prepare the syringe carefully as follows

The pre-filled syringe is for single patient only. Discard syringe after use. DO NOT REUSE.

The content of un-opened and un-damaged blister is sterile, and must not be opened until use.

2025.06.17

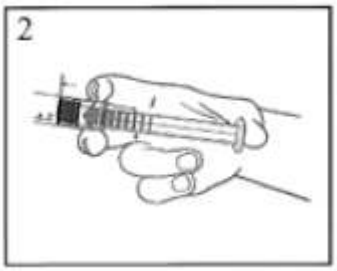
The product should be inspected visually for particles and discoloration prior to administration. Only clear colourless solution free from particles or precipitates should be used.

The product should not be used if the tamper evident seal on the syringe is broken.

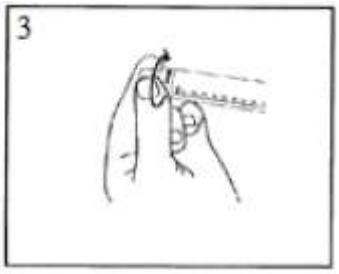
The external surface of the syringe is sterile until the blister is opened.

When handled using an aseptic method, Phenylephrine 50 µg/mL PS Equity, solution for injection in pre-filled syringe can be placed on a sterile field.

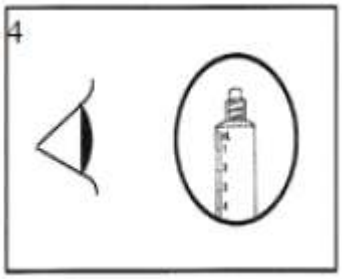
1) Withdraw the pre-filled syringe from the sterile blister.



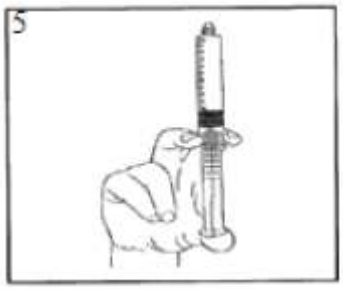
2) Push on the plunger to free the bung. The sterilisation process may have caused adhesion of the bung to the body of the syringe.



3) Twist off the end cap to break the seal. In order to avoid contamination, do not touch the exposed luer connection.



4) Check that the syringe seal tip has been completely removed. If not, replace the cap and twist again



5) Expel the air by gently pushing the plunger.

6) Connect the syringe to the IV access. Push the plunger slowly to inject the required volume.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Equity Pharmaceuticals (Pty) Ltd

100 Sovereign Drive

Route 21 Corporate Park

Nellmapius Drive

Irene, Pretoria

8. REGISTRATION NUMBER(S)

57/6.1/0540

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

17 June 2025

2025.06.17

10. DATE OF REVISION OF THE TEXT

2025.06.17