

Equity Pharmaceuticals (Pty) Ltd
Phenylephrine 50 µg/mL PS Equity, Solution for Injection in
prefilled syringe
Each mL contains phenylephrine hydrochloride equivalent to
50 micrograms of phenylephrine
Application no.: 570540

Approved Professional Information
Approval Date : 17 June 2025

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

Method of administration

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

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.

Arterial blood pressure should be monitored during treatment.

- 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.

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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.

Contraindicated combinations (see section 4.3)

- 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.

- Increased risk of vasoconstriction and / or hypertensive crisis.

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Increased risk of vasoconstriction and/or hypertensive crisis.

- Increased risk of vasoconstriction and/or hypertensive crisis.

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

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

- *Noradrenergic-serotonergic 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

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

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.

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.

- *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

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

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

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

* 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.

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 adenylyl cyclase, whereas beta-adrenergic effects result from stimulation of adenylyl 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.

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.

Absorption

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

Distribution

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)

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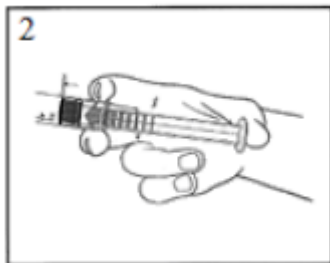
The product should be inspected visually for particles and discoloration prior to administration. Only clear colourless solution free from particles or precipitates should be used.

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

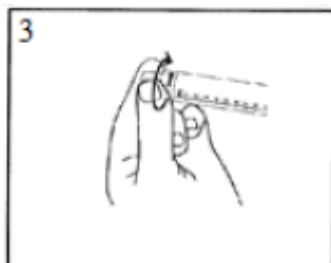
The external surface of the syringe is sterile until the blister is opened.

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.

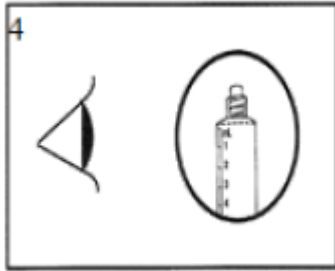
1) Withdraw the pre-filled syringe from the sterile blister.



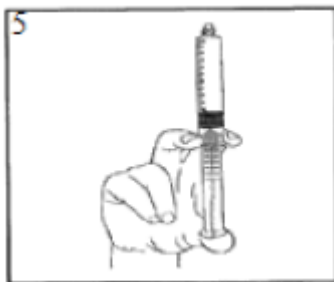
2) Push on the plunger to free the bung. The sterilisation process may have caused adhesion of the bung to the body of the syringe.



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

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