Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Phenylephrine Hydrochloride 10 mg/ml solution for injection/infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml of solution for injection contains 10 mg phenylephrine hydrochloride equivalent to 8.2 mg phenylephrine.
Each 1 ml ampoule contains 10 mg phenylephrine hydrochloride equivalent to 8.2 mg phenylephrine.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection/infusion.
Clear, colourless, sterile solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of hypotensive states during spinal anaesthesia or drug-induced hypotension.

4.2 Posology and method of administration

Posology
Each 1 ml ampoule contains 10 mg phenylephrine hydrochloride equivalent to 8.2 mg phenylephrine. Dosing of this medicinal product is given in units of phenylephrine hydrochloride rather than in units of phenylephrine which differs from other similar authorised products. Recommended intravenous dosing regimens also vary between formulations. Please take special note of the presentation and concentration of the product and adjust your administration practices accordingly.

Adults
Subcutaneous and intramuscular injection
Phenylephrine injection may be administered subcutaneously or intramuscularly in a dosage of 2 to 5 mg with further doses of 1 to 10 mg if necessary according to response.

Intravenous bolus injection:
Phenylephrine hydrochloride injection may be administered in a dose of 100 to 500 micrograms by slow intravenous injection as a 0.1% w/v solution, repeated as necessary after at least 15 minutes. See instructions on dilution in section 6.6.

Continuous infusion:
10 mg in 500 ml of glucose 5% w/v injection or sodium chloride 0.9% w/v injection may be infused intravenously, initially at a rate of up to 180 micrograms per minute, reduced according to response to 30-60 micrograms per minute. See instructions on dilution in section 6.6.

Renal impairment
Lower doses of phenylephrine may be needed in patients with impaired renal function.

Hepatic Impairment
Higher doses of phenylephrine may be needed in patients with cirrhosis of the liver.

Elderly
There is no need for dosage reduction in the elderly. Treatment of the elderly should be carried out with care.

Children
100 micrograms/kg bodyweight subcutaneously or intramuscularly.

Method of administration
For subcutaneous, intramuscular or intravenous bolus injection, or intravenous infusion.

For instructions on dilution of the medicinal product before administration, see section 6.6.

This medicine should only be administered by healthcare professionals with appropriate training and relevant experience.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Patients taking non-selective monoamine oxidase inhibitors (MAOIs), or within 14 days of ceasing such treatment due to risk of paroxysmal hypertension and possibly fatal hyperthermia (see section 4.5).
- Patients with severe hypertension.
- Patients with severe hyperthyroidism.
- Patients with peripheral vascular disease due to the risk of ischemic gangrene or vascular thrombosis.

4.4 Special warnings and precautions for use

Special caution should be exercised when administering phenylephrine to patients with pre-existing cardiovascular disease such as ischaemic heart disease, arrhythmias, arterial hypertension, aneurysms, or non- severe peripheral vascular insufficiency. Anginal pain may be precipitated in patients with angina pectoris.

Caution should also be exercised when phenylephrine is administered to patients with diabetes mellitus or closed- angle glaucoma.

Phenylephrine can induce a reduction in cardiac output. Consequently, it must be administered with extreme caution to patients with arteriosclerosis, to elderly and to patients with impaired cerebral or coronary circulation.

In patients with reduced cardiac output 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.

In patients with serious heart failure or cardiogenic shock, phenylephrine 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 injection to avoid extravasation, since this may cause tissue necrosis.

Phenylephrine may cause urinary retention and patients with prostatic hypertrophy may experience increased difficulty with micturition (see section 4.8).

To be used with caution in patients with phaeochromocytoma.

4.5 Interaction with other medicinal products and other forms of interaction

Contraindicated combinations (see section 4.3)

• Non-selective MAOIs:
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.

Inadvisable combinations (see section 4.4)

• Dopaminergic ergot alkaloids (bromocriptine, cabergoline, lisuride, pergolide):
Risk of vasoconstriction and/or hypertensive crisis.

• Vasoconstrictor ergot alkaloids (dihydroergotamine, ergotamine, methylergometrine, methysergide):
Risk of vasoconstriction and/or hypertensive crisis.

• Tricyclic antidepressants (e.g. imipramine):
Paroxysmal hypertension with possibility of arrhythmias (inhibition of adrenaline or noradrenaline entry in sympathetic fibres).

• Noradrenergic-serotoninergic antidepressants (milnacipran, venlafaxine):
Paroxysmal hypertension with possibility of arrhythmias (inhibition of adrenaline or noradrenaline entry in sympathetic fibres).

• Selective type A MAOIs:
Risk of vasoconstriction and/or hypertensive crisis.

• Linezolid:
Risk of vasoconstriction and/or hypertensive crisis.

• Antihypertensive agents (e.g. 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 agents.

• Cardiac glycosides, quinidine:
Increased risk of arrhythmias.

• Sibutramine:
Paroxysmal hypertension with possibility of arrhythmias (inhibition of adrenaline or noradrenaline entry in sympathetic fibres).

• Halogenated volatile anaesthetics (cyclopropane, halothane, desflurane, enflurane, isoflurane, methoxyflurane, sevoflurane):
Risk of perioperative hypertensive crisis and arrhythmia.

Phenylephrine can interact with cyclopropane and halothane and other halogenated inhalational anaesthetics, which can induce ventricular fibrillation.

Combinations requiring precautions for use:

• Oxytocic agents:
The effect of presso-active sympathomimetic amines is potentiated. Thus, some oxytocic agents may cause severe persistent hypertension and strokes can occur during post-partum period.

• Alpha and beta-receptor blocking drugs:
Interactions of phenylephrine with alpha and beta receptor blocking drugs may be complex.

4.6 Fertility, pregnancy and lactation

Pregnancy
The safety of phenylephrine during pregnancy and lactation has not been established. Administration of phenylephrine in the later stages of pregnancy or during childbirth may cause fetal hypoxia and bradycardia.
Excretion of phenylephrine hydrochloride into breast milk appears to be minimal.

Breast-feeding
The safety of phenylephrine during lactation has not been established.
Small quantities of phenylephrine are excreted in human breast milk and oral bioavailability may be low. Administering vasoconstrictors to the mother exposes the neonate to a theoretical risk of cardiovascular and neurological effects. However, in the event of a single bolus administration during childbirth, breast-feeding is possible.

Fertility
There is no available data concerning fertility after exposure to phenylephrine (see section 5.3).

4.7 Effects on ability to drive and use machines

No adverse effects known.

4.8 Undesirable effects

Adverse reactions can be classified according to the frequency of the disorder as: Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000), not known (cannot be estimated from the available data).

During the use of Phenylephrine, the following adverse reactions have been observed, the frequency of which have not been accurately established:

Cardiac disorders:
Reflex bradycardia, reflex tachycardia, cardiac arrhythmias, anginal pain, palpitations, cardiac arrest.

Vascular disorders:
Hypertension, hypotension, flushing.

Nervous system disorders:
Headache, cerebral haemorrhage, vertigo, fainting, head discomfort.

Phenylephrine lacks significant stimulant effects on the central nervous system at usual doses.

Respiratory,thoracic and mediastinal disorders:
Dyspnoea, pulmonary oedema.

Gastrointestinal disorders:
Vomiting, salivary hypersecretion.

Renal and urinary disorders:
Difficulty in urination, urinary retention.

Skin and subcutaneous tissue disorders:
Sweating, temporary tingling, cold feeling on the skin.

Metabolism and nutrition disorders:
Alterations in glucose metabolism.

General disorders and administration site conditions:
Extravasation of phenylephrine can cause tissue necrosis.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance Website: www.hpra.ie

4.9 Overdose

Symptoms
Symptoms of overdosage include headache, vomiting, hypertension and reflex bradycardia and other cardiac arrhythmias.

Management
Treatment should consist of symptomatic and supportive measures. The hypertensive effects may be treated with an alpha-adrenoceptor blocking drug, such as phentolamine.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Adrenergic and dopaminergic agents, ATC code: C01C A06.

Phenylephrine hydrochloride is a sympathomimetic agent with mainly direct effects on adrenergic receptors. It has predominantly alpha-adrenergic activity and is without significant stimulating effects on the central nervous system at usual doses. After injection it produces peripheral vasoconstriction and increased arterial pressure. It also causes reflex bradycardia.

5.2 Pharmacokinetic properties

Distribution
When injected subcutaneously or intramuscularly, phenylephrine takes 10 to 15 minutes to act. Subcutaneous and intramuscular injections are effective for up to about one and up to two hours respectively. Intravenous injections are effective for up to about 20 minutes.

Biotransformation
Phenylephrine is metabolised in the liver by monoamine oxidase.

Elimination
The metabolites, their route and rate of excretion have not been identified.

5.3 Preclinical safety data

No data are available on safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, fertility, or toxicity to reproduction.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium hydroxide
Hydrochloric acid
Water for injection

6.2 Incompatibilities

Phenylephrine has been stated to be incompatible with alkalis, ferric salts, phenytoin sodium and oxidising agents. In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

Unopened: 3 years.

After opening and dilution: Chemical and physical in-use stability has been demonstrated for 24 hours at room temperature. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2-8°C.

6.4 Special precautions for storage

Store below 25°C. Store in the original package.

6.5 Nature and contents of container

Type 1 amber glass ampoule with ceramic break ring.
Pack size: 10 ampoules

6.6 Special precautions for disposal and other handling

Solution with a high concentration that must be diluted before IV injection or infusion administration.

Dilution:
Phenylephrine Hydrochloride 10 mg/ml solution for Injection or Infusion can be administered as an intravenous injection or infusion after dilution in glucose 5% w/v solution or sodium chloride 0.9% w/v solution.

To prepare the required concentration, dilute as follows:

Concentration of solution to be administered	Volume of 10 mg/ml solution	Volume of diluent solution
20 micrograms/ml	1 ml	500 ml
50 micrograms/ml	1 ml	200 ml
100 micrograms/ml	1 ml	100 ml
1 mg/ml (0.1% w/v)	1 ml	10 ml

Any unused medicinal product or waste material should be disposed of in accordance with local requirements. For single use only.
This medicine should be inspected for particles or discoloration prior to administration. This medicine should not be used if the solution is coloured or contains particles.
Discard any unused contents.

7 MARKETING AUTHORISATION HOLDER

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D04 C5Y6
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8 MARKETING AUTHORISATION NUMBER

PA1418/011/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 4th November 2022

10 DATE OF REVISION OF THE TEXT

November 2023