SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Phenylephrine 0.1 mg/ml, solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One ml of Phenylephrine 0.1 mg/ml, solution for injection, contains phenylephrine hydrochloride equivalent to 0.1 mg of phenylephrine.

- Each 5 ml ampoule of Phenylephrine 0.1 mg/ml contains phenylephrine hydrochloride equivalent to 0.5 mg phenylephrine.

- Each 10 ml ampoule of Phenylephrine 0.1 mg/ml contains phenylephrine hydrochloride equivalent to 1.0 mg phenylephrine.

Excipient with known effect:

Each 10 ml ampoule contains 1,6 mmol (36,8 mg) sodium.

Each 5 ml ampoule contains 0,8 mmol (18,4 mg) sodium.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.

Clear, colourless solution with an osmolality of 270-300 mOsm/kg.

pH: 4,5-6,5.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of hypotension during spinal, epidural and general anaesthesia.

4.2 Posology and method of administration

Posology

Adults

Intravenous bolus injection:

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

Continuous infusion:

Initial dose is 25 to 50 micrograms/min. The doses may be increased or decreased to maintain the systolic blood pressure close to the normal value. Doses between 25 and 100 micrograms/min have been assessed to be effective.

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.

Older people:

Treatment of the elderly should be carried out with care.

Paediatric population:

The safety and efficacy of phenylephrine in children have not been established. No data are available.

Method of administration**:**

Parenteral administration. Intravenous bolus injection or intravenous infusion.

Phenylephrine, 50 micrograms/ml and 100 micrograms/ml, solution for injection, should only be administered by health care professionals with appropriate training and relevant experience.

4.3 Contraindications

Phenylephrine should not be used

- in patients with hypersensitivity to the active substance or to any of the excipients listed in section 6.1;

- in patients with severe hypertension or peripheral vascular disease due to the risk of ischemic gangrene or vascular thrombosis;

- in combination with non-selective monoamine oxidase inhibitors (MAOs) (or within 2 weeks of their withdrawal) due to the risk of paroxysmal hypertension and possibly fatal hyperthermia (see section 4.5);

- in patients with severe hyperthyroidism.

4.4 Special warnings and precautions for use

The arterial blood pressure should be monitored during treatment.

Phenylephrine should be administered with care to patients with:

- diabetes mellitus;
- arterial hypertension;
- uncontrolled hyperthyroidism;
- coronary heart disease and chronic heart conditions;
- non-severe pheripheral vascular insufficiency;
- bradycardia;
- partial heart block;
- tachycardia;
- arrhythmias;
- angina pectoris (phenylephrine can precipitate or exacerbate angina in patients with coronary artery disease and history of angina);
- aneurysma;
- closed angle glaucoma;

Phenylephrinecan induce a reduction in cardiac output. Therefore, care should be exercised in administeringto patients with arteriosclerosis, the 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 to phenylephrine injection to avoid extravasation, since this may cause tissue necrosis.

This medicinal product contains 36.8 mg (1.6 mmol) sodium in each 10 ml ampoule , equivalent to 1,8% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

Each 5 ml ampoule contains 0,8 mmol (18,4 mg) sodium, i.e. essentially sodium-free.

4.5 Interaction with other medicinal products and other forms of interaction

Contraindicated combinations (see section 4.3):
- Non-selective monoamine oxidase inhibitors (MAOs) (iproniazid, nialamide):

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

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

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

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

Risk of vasoconstriction and/or hypertensive crisis.

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

- Guanethidine and related products:
Substantial increase in blood pressure (hyper reactivity linked to the reduction in sympathetic tone and /or to the inhibition of adrenaline or noradrenaline entry in sympathetic fibers). If the combination cannot be avoided, use with caution lower doses of sympathomimetic agents.

- Cardiac glycosides, quinidine:
Increased risk of arrhythmias.

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

Combinations requiring precautions for use:

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

4.6 Fertility, Pregnancy and lactation

Pregnancy

Animal studies are insufficient with respect to reproductive toxicity and teratogenicity (see section 5.3). Administration of phenylephrine in late pregnancy or labour may potentially cause fetal hypoxia and bradycardia. Use of injectable phenylephrine is possible during pregnancy in accordance with the indications.

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

Breastfeeding
Small quantities of phenylephrine are excreted into human breast milk and oral bioavalability may be low. Administering vasoconstricors to the mother exposes the infant to a theroretical 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 (se section 5.3).

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

Summary of the safety profile

The most common adverse events of phenylephrine are bradycardia, hypertensive episodes, nausea and vomiting. Hypertension is more frequent with high doses.

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

List of adverse reactions

Frequency: Not known (cannot be estimated from available data)

Immune system disorders:

Not known: Hypersensitivity

Psychiatric disorders:

Not known: Anxiety, excitability, agitation, psychotic states, confusion

Nervous system disorders:

Not known: Headache, nervousness, insomnia, paresthesia, tremor

Eye disorders:

Not known: Mydriasis, aggravation of pre-existing angle-closure glaucoma

Cardiac disorders:

Not known: Reflex bradycardia, tachycardia, palpitations, hypertension, arrhythmia, angina pectoris, myocardial ischemia

Vascular disorders:

Not known: Cerebral haemorrhage, hypertensive crisis

Respiratory, thoracic and mediastinal disorders:

Not known: Dyspnoea, pulmonary oedema

Gastrointestinal disorders:

Not known: Nausea, vomiting

Skin and subcutaneous tissue disorders:

Not known: Sweating, pallor or skin blanching, piloerection, skin necrosis with extravasation

Musculoskeletal and connective tissue disorders:

Not known: Muscular weakness

Renal and urinary disorders:

Not known: Difficulty in micturition and urinary retention

Description of selected adverse reactions

As phenylephrine 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.

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 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 the Yellow Card Scheme at www.mhra.gov.uk/yellowcard.

4.9 Overdose

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

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 drugs. ATC code: C01C A06

Mechanism of action

Phenylephrine is a potent vasoconstrictor that acts almost exclusively by stimulation of alpha-1-adrenergic receptors. Arterial vasoconstriction is accompanied by venous vasoconstriction which gives an increase in blood pressure and reflex bradycardia. The potent arterial vasoconstriction results in an increase in the resistance which results in reduction of the cardiac output. This is less pronounced in healthy people, but can be exacerbated in the case of previous heart failure.

5.2 Pharmacokinetic properties

The duration is 20 minutes after an intravenous administration.

Plasma protein binding is unknown.

Distribution

The distribution volume after a single dose is 340 litres.

Elimination and biotransformation

Phenylephrine is primarily excreted by the kidneys as m-hydroxy mandelic acid and phenol conjugates.

Special patient populations
There are no pharmacokinetic data available in special patient populations.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the assessment of safety, in addition to that already presented in this Summary of product characteristic.

Animal studies are insufficient to evaluate the effects on fertility and reproduction.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride, sodium citrate, citric acid, water for injection and hydrochloride acid and sodium hydroxide for pH adjustment.

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Keep the ampoules in the outer carton in order to protect from light.

6.5 Nature and contents of container

Phenylephrine 0.1 mg/ml: 5 ml and 10 ml glass ampoules in packages of 5, 10, 20, 50 or 100 ampoules.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

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

7 MARKETING AUTHORISATION HOLDER

Unimedic Pharma AB

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SE-102 34 Stockholm

Sweden

8 MARKETING AUTHORISATION NUMBER(S)

PL 50604/0002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

09/04/2025

10 DATE OF REVISION OF THE TEXT

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