SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Phenylephrine Unimedic 10 mg/ml, concentrate for solution for injection/infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One ml of Phenylephrine Unimedic 10 mg/ml, concentrate for solution for injection/infusion, contains phenylephrine hydrochloride equivalent to 10 mg of phenylephrine.

- Each 2 ml ampoule (containing 1 ml solution) of Phenylephrine Unimedic 10 mg/ml contains phenylephrine hydrochloride equivalent to 10 mg of phenylephrine.

Excipient with known effect:

Each 2 ml ampoule (containing 1 ml solution) contains 0,2 mmol (3,7 mg) sodium.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Concentrate for solution for injection/infusion, [sterile concentrate]

Clear and colourless solution. 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

To be administered by intravenous injection or infusion. Whenever solution and container permit, parenteral drug products should be inspected visually for particulate matter and discolouration prior to administration.

This product should be administered after appropriate dilution. See section 6.6 for Instructions on dilution.

Adults

Intravenous bolus injections:

Initially repeated bolus doses of 50 to 100 micrograms (1-2 ml of the 50 micrograms/ml diluted solution or 0,5-1 ml of the 100 micrograms/ml diluted solution) are given until the desired effect is attained and before the continuous infusion is started. See instructions on dilution in section 6.6)

Continuous infusion:

Large dose variations occur. Initial dose is commonly in the range of 25 to 50 micrograms/min. The doses may subsequently be increased or decreased to maintain the systolic blood pressure close to the normal (target) value. Doses between 25 to 100 micrograms/min have been assessed to be effective.

If doses higher than 50 micrograms/min are required or there is a tendency to reflex bradycardia a switch to another vasopressor drug should be done.
The blood pressure must be monitored regularly.

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.

10 mg/ml: concentrate for dilution to injections or infusion.

Phenylephrine, 10 mg/ml, should only be administered by health care professionals with appropriate training and relevant experience.

Ensure that the needle is correctly inserted and avoid extravasation because of the risk of tissue damage/ ischemia.

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

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;

Phenylephrine 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 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.

Each 2 ml ampoule (containing 1 ml solution) contains 0,2 mmol (3,7 mg) sodium per ampoule, i.e. is 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 fibres).

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

- 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. Phenylephrine Unimedic is not recommended during pregnancy..

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 reported in literature are bradycardia, hypertensive episodes, nausea and vomiting. Most undesired effects of phenylephrine are dose dependent.

Tabulated summary of adverse reactions

The adverse reactions listed by system organ class and frequency. Frequencies: not known (cannot be estimated from the available data)

Table 1 Tabulated list of Adverse reactions

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 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 national reporting system listed in Appendix V.

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 injections and hydrochloric acid and sodium hydroxide for pH adjustment.

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life

Unopened:

2 years.

After opening and dilution:
Chemical and physical in-use stability has been demonstrated for 7 days at room temperature (20-25°C).
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 to 8°C, unless dilution has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

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

For storage conditions after dilution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

2 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

Solution with a high concentration and that must be diluted before the administration.

Reconstitution/dilution:

Phenylephrine Unimedic 10 mg/ml will be administered as an intravenous injection or infusion after dilution in sodium chloride 9 mg/ml (or glucose 50 mg/ml).

- Dilution to a concentration of 100 micrograms/ml: 1 ml of the 10 mg/ml solution is diluted in 100 ml

  sodium chloride 9 mg/ml (or glucose 50 mg/ml).

- Dilution to a concentration of 50 micrograms/ml: 1 ml of the 10 mg/ml solution is diluted in 200 ml

  sodium chloride 9 mg/ml or glucose 50 mg/ml.

Other concentrations may also occur.

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

7 MARKETING AUTHORISATION HOLDER

Unimedic Pharma AB

PO Box 6216

SE-102 34 Stockholm

Sweden

8 MARKETING AUTHORISATION NUMBER(S)

PL 50604/0003

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

09/04/2025

10 DATE OF REVISION OF THE TEXT

09/04/2025