# PHENYLALPHA® 50 micrograms/ml
# Solution for injection
### Phenylephrine

## 1. NAME OF THE MEDICINAL PRODUCT

PHENYLALPHA® 50 micrograms/ml, solution for injection

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Phenylephrine..... 50.00 micrograms
In the form of phenylephrine hydrochloride ..... 60.90 micrograms
For 1 ml
One 10-ml ampoule contains 500 micrograms of phenylephrine (in the form of phenylephrine hydrochloride).
Excipients with known effect: sodium.
One ml of solution for injection contains 3.72 mg of sodium, equivalent to 0.162 mmol.
One 10 ml ampoule contains 37.2 mg of sodium, equivalent to 1.62 mmol.
For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Solution for injection.
Clear colourless solution.
pH: 4.7 - 5.3
Osmolality: 270-300 mOsm/Kg

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Treatment of hypotension during general anaesthesia and locoregional anaesthesia, whether spinal or epidural, and whether for surgical or obstetric procedures.
Preventive treatment of hypotension during spinal anaesthesia for surgical or obstetric procedures.

### 4.2 Posology and method of administration

**Posology**

*Intravenous bolus injection*
Normal dose is 50 to 100 micrograms, which can be repeated until the desired effect is attained. The doses may be increased in the case of severe hypotension, but must not exceed a bolus of 100 micrograms.

*Continuous infusion*
Initial dose is 25 to 50 micrograms/min. Doses can be increased up to 100 micrograms/min or reduced in order to maintain systolic blood pressure close to its reference value.
Doses between 25 and 100 micrograms/min have been considered effective in maintaining maternal blood pressure.

*Renal impairment*
Lower doses of PHENYLALPHA® may be needed in patients with impaired renal function.

*Hepatic Impairment*
Higher doses of PHENYLALPHA® 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.
PHENYLALPHA® 50 micrograms/ml, solution for injection should only be administered by healthcare professionals with appropriate training and relevant experience.

### 4.3 Contraindications

PHENYLALPHA® should not be used:
- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1;
- in combination with non-selective monoamine oxidase inhibitors (MAOs) (or within 2 weeks of their withdrawal) due to risk of paroxysmal hypertension and possibly fatal hyperthermia (see section 4.5);
- in patients with severe hypertension or peripheral vascular disease due to the risk of ischemic gangrene or vascular thrombosis;
- in patients with severe hyperthyroidism.

### 4.4 Special warnings and precautions for use

The venous and arterial blood pressure should be monitored during treatment.
PHENYLALPHA® should be administered with care to patients with:
- diabetes mellitus;
- arterial hypertension;
- uncontrolled hyperthyroidism;
    - coronary heart disease and chronic heart conditions;
    - non-severe peripheral 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. 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 to Phenylephrine injection to avoid extravasation, since this may cause tissue necrosis.
This medicinal product contains 37.2 mg sodium per ampoule, equivalent to 1.9 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.

### 4.5 Interaction with other medicinal products and other forms of interaction

*Contraindicated combinations (see section 4.3)*
• Non-selective MAO inhibitors
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, 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 MAO inhibitors
Risk of vasoconstriction and/or hypertensive crisis.
• Linezolid:
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 fibers). 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 fibers).
• 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 is 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).

**Breast-feeding**

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.

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**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**

This medicinal product is not compatible with driving a vehicle or operating machinery.

**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.
Bradycardia is 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).

**4.9 Overdose**

Symptoms of overdose include headache, nausea, vomiting, paranoid psychosis, hallucinations, hypertension and reflex bradycardia. Cardiac arrhythmia such as ventricular extrasystoles 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: CARDIAC STIMULANT EXCEPT CARDIAC GLYCOSIDES, ATC Code: C01CA06**

Phenylephrine is a potent vasoconstrictor that acts almost exclusively by stimulating alpha-1-adrenergic receptors.
Such arterial vasoconstriction is also accompanied by venous vasoconstriction. This gives an increase in blood pressure and reflex bradycardia. The potent arterial vasoconstriction gives an increase in the systemic vascular resistance (increase in afterload). The overall result is a reduction in the cardiac output. This is less pronounced in healthy people but it may worsen in cases of previous heart failure. As Phenylephrine effects are linked to its pharmacological properties, they can be controlled by known antidotes.

**5.2 Pharmacokinetic properties**

The volume of distribution after single dose is 340 litres.
Phenylephrine is metabolised in the liver by monoamine oxidase.
Phenylephrine is mainly excreted via the kidneys as m-hydroxymandelic acid and phenol conjugates.
The duration of effect is 20 minutes after intravenous administration.
The terminal half life of injectable phenyleprine is about 3 hours.
The plasma protein binding is unknown.
There is no data available on the pharmacokinetics in special patient groups.

**5.3 Preclinical safety data**

Available non clinical data do not bring to the prescriber any additional relevant information in comparison with those already mentioned in the other sections of the SPC.
Animal studies are insufficient to evaluate effects on fertility and reproduction.

## 6. PHARMACEUTICAL PARTICULARS

**6.1 List of excipients**

Sodium chloride, sodium citrate dihydrate, citric acid monohydrate, sodium hydroxide (for pH adjustment), water for injection.

**6.2 Incompatibilities**

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

**6.3 Shelf life**

3 years.

**6.4 Special precautions for storage**

Store the ampoules in their original packaging, away from light. Do not store above 30°C.

**6.5 Nature and contents of container**

10 ml solution in ampoule (polypropylene). Boxes of 10.

**6.6 Special precautions for disposal and other handling**

No special requirements.

## 7. PRODUCT OWNER

Laboratoire AGUETTANT
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## 8. DATE OF REVISION OF THE TEXT

**January 2022**