SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product

Phenylephrine Sintetica 10 mg/ml solution for injection or

infusion.

2. Qualitative and quantitative composition

Each 1 ml ampoule contains 10 mg

phenylephrine hydrochloride.

For the full list of excipients, see section 6.1

3. Pharmaceutical form

Solution for injection or infusion, Clear, colorless solution.

4. Clinical particulars

4.1 Therapeutic indications

For the treatment of hypotensive states, e.g. septic shock, circulatory failure, during spinal anaesthesia or drug-induced hypotension

4.2 Posology and method of administration

For subcutaneous, intramuscular or slow intravenous injection or by intravenous infusion.

Whenever solution and container permit, parenteral drug products should be inspected visually for particulate matter and discolouration prior to administration.

Adults

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, or in a dose of 100 to 500 micrograms by slow intravenous injection as a 0.1% solution, repeated as necessary after at least 15 minutes.

Alternatively, 10 mg in 500 ml of glucose 5% injection or sodium chloride 0.9% 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.

Children

100 micrograms/kg bodyweight subcutaneously or intramuscularly.

Elderly

There is no need for dosage reduction in the elderly.

4.3 Contraindications

Hypersensitivity to phenylephrine or to any of the excipients listed in section 6.1.

Patients taking monoamine oxidase inhibitors, or within 14 days of ceasing such treatment.

Severe hypertension and hyperthyroidism.

Avoid in patients with prostatic enlargement.

t

4.4 Special warnings and precautions for use

Great care should be exercised in administering Phenylephrine Injection to patients with pre-existing cardiovascular disease such as ischaemic heart disease, arrhythmias, occlusive vascular disease including arteriosclerosis, hypertension or aneurysms. Anginal pain may be precipitated in patients with angina pectoris.

Care is also required when given to patients with diabetes mellitus or closed-angle

glaucoma. Keep all medicines out of the reach of children.

4.5 Interaction with other medicinal products and other forms of interaction

Phenylephrine may interact with cyclopropane and halothane and other halogenated inhalational anaesthetics, to induce ventricular fibrillation.

An increased risk of arrhythmias may also occur if phenylephrine injection is given to patients receiving cardiac glycosides, quinidine or tricyclic antidepressants.

Phenylephrine may increase blood pressure and consequently reverse the action of many antihypertensive agents.

Interactions of phenylephrine with alpha and beta receptor blocking drugs may be complex. Drugs which have an effect on α_1- adrenoreceptors could potentiate (such as ganisetron or clonidine) or inhibit (such as doxazosin or buspirone) the vasopressive action of phenylephrine.

Caution should be applied when administering atomoxetine concurrently, as there is potential for synergistic pharmacological effects.

Severe hypertension may occur following the use of phenylephrine and atropine or other antimuscarinics.

The pressor effects of phenylephrine may be slightly reduced by lithium carbonate.

The effects of phenylephrine may be potentiated by the use of monoamine oxidase inhibitors or reversible inhibitors of monoamine oxidase.

4.6 Pregnancy, labor and lactation

The safety of phenylephrine during pregnancy and lactation has not been established.

The most common maternal adverse reactions reported in published studies of phenylephrine use during neuraxial anesthesia during Cesarean delivery include nausea and vomiting, bradycardia, reactive hypertension, and transient arrhythmias. Phenylephrine, when administered during labor or delivery, does not appear to alter either neonatal Apgar scores or umbilical artery blood-gas status

Excretion of phenylephrine in breast milk appears to be minimal.

4.7 Effects on ability to drive and use machines

No adverse effects known.

4.8 Undesirable effects

The frequency for the following adverse reactions is unknow (cannot be estimated from the available data):

Immune system disorders

Hypersensitivity

Metabolism and nutrition disorders

Metabolic disorders

Psychiatric disorders

Nervousness, insomnia

Nervous system disorders

Headache, cerebral haemorrhage, paraesthesia

Eye disorders

Mydriasis, angle-closure glaucoma

t

Cardiac disorders

Pulmonary oedema, bradycardia, tachycardia, arrhythmia, angina pectoris, palpitations, cardiac arrest

Vascular disorders

Hypotension, dizziness, syncope, flushing

Respiratory, thoracic and mediastinal disorders

Dyspnoea

Gastrointestinal disorders

Vomiting, salivary hypersecretion

Renal and urinary disorders

Dysuria, urinary retention

General disorders and administration site conditions

Extravasation, infusion site necrosis, hyperhidrosis

Investigations

Increased blood pressure, abnormal blood glucose

Phenylephrine is without significant stimulating effects on the central nervous system at usual doses.

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. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form
https://sideeffects.health.gov.il

4.9 Overdose

Symptoms of overdosage include headache, vomiting, hypertension and reflex bradycardia and other cardiac arrhythmias. In severe cases confusion, hallucinations and seizures 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 to 60 mg i.v. over 10-30 minutes, repeated as necessary

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

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. Phenylephrine is metabolised in the liver by monoamine oxidase. The metabolites, their route and rate of excretion have not been identified.

5.3 Preclinical safety data

Phenylephrine has been used to induce cardiac myocyte hypertrophy in cultures of rat neonatal mycocytes at doses of 100 µM and 10 µM. To the best of our knowledge there have been no human studies associating therapeutic phenylephrine use with the development of cardiac myocyte hypertrophy.

t

6. Pharmaceutical particulars

6.1 List of excipients

Sodium chloride

1 N Hydrochloric Acid

Water for Injections

6.2 Incompatibilities

Phenylephrine Injection has been stated to be incompatible with alkalis, ferric salts, phenytoin sodium and oxidising agents.

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials

After dilution:
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.

6.4 Special precautions for storage

Keep out of sight and reach of children.

Store below 25°C. Do not refrigerate or freeze. This product is only for a

single use.

6.5 Nature and contents of container

Type I one point cut clear colourless glass 2 ml ampoules.

Box of 10 ampoules containing 1 ml of solution for injection.

6.6 Special precautions for disposal and other handling

Phenylpehrine Sintetica 10mg/ml solution for injection/infusion can be diluted with the following solutions: Glucose 5%, Sodium chloride 0.9%

7. Marketing authorisation holder

CTS Ltd.,
4 Haharash St., Hod-Hasharon, 4524075.

8. Marketing authorization number

163-12-35465

9. Manufacturer

Sintetica SA
Via Penate 5, CH-6850 Mendrisio,
Switzerland

This leaflet from January 2020 is in the format determined by the Ministry of Health and its content is compatible with the leaflet of the original product, that was checked and approved by the MoH in June 2019

t