

## Professional Information for RUSAINE 10 mg/mL

### SCHEDULING STATUS

**S1**

#### 1. NAME OF THE MEDICINE

**RUSAINE 10 mg/mL** solution for injection/infusion

#### 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 mL contains 10 mg phenylephrine hydrochloride.

*Excipients with known effect:*

Contains sodium metabisulphite (2 mg per 1 mL).

Sugar free.

For the full list of excipients, see section 6.1.

#### 3. PHARMACEUTICAL FORM

Solution for injection/infusion.

A clear, colourless solution.

#### 4. CLINICAL PARTICULARS

##### 4.1 Therapeutic indications

RUSAINE is indicated for increasing the blood pressure in adults with clinically significant hypotension resulting primarily from vasodilation, in such settings as septic shock or anaesthesia.

The duration of action is short-lived (minutes) and repeat injections are frequently required.

##### 4.2 Posology and method of administration

*General dosing information*

Patients receiving RUSAINE should be closely monitored. Treatment with RUSAINE is not a substitute for replacement of blood, plasma, fluids and/or electrolytes.

Prior to administration of therapy, hypovolaemia should be corrected. Acidosis may reduce the effectiveness of RUSAINE. An infusion pump or other suitable metering device should be used to control the rate of infusion in order to avoid unintended administration of a bolus dose. Infusions of RUSAINE should be given into a large vein, or preferably, directly into the central venous line. Inspect the solution for particulate matter and discolouration prior to administration. Discard any unused portion.

RUSAINE is not for intramuscular or subcutaneous use.

Caution is recommended to avoid extravasation, which may cause tissue necrosis and sloughing of surrounding tissues (see section 4.4). When discontinuing therapy, the dosage should be reduced gradually, since sudden cessation of therapy may result in severe hypotension.

Intravascular fluid should be replaced if necessary, to avoid hypotension.

RUSAINE must be diluted before administration as bolus intravenous infusion or continuous intravenous infusion. Dosage must be adjusted to meet the individual requirements of each patient, on the basis of clinical response. Some patients may need higher than usual recommended doses for a time.

## **Posology**

### **Adults**

#### ***Preparing a 50 mcg/mL solution of bolus intravenous administration***

For bolus intravenous administration, add 10 mg (1 mL of a 10 mg/mL concentration) of RUSAINE to 200 mL of 5 % dextrose injection or 0,9 % sodium chloride injection. This will yield a final concentration of 50 mcg/mL. Withdraw an appropriate dose from the 50 mcg/mL solution prior to bolus intravenous administration of the diluted solution.

### ***Preparing a solution for continuous intravenous infusion***

For continuous intravenous infusion, withdraw 10 mg (1 mL of 10 mg/mL concentration) of RUSAINÉ and add 500 mL of 5 % dextrose injection or 0,9 % sodium chloride injection (providing a final concentration of 20 mcg/mL).

### ***Dosing for perioperative setting***

In adult patients undergoing surgical procedures with either neuraxial anaesthesia or general anaesthesia:

- 50 mcg to 250 mcg by intravenous bolus administration. The most frequently reported initial bolus dose is 50 mcg or 100 mcg.
- 0,5 mcg/kg/min to 1,4 mcg/kg/min by intravenous continuous infusion, titrated to blood pressure goal.

### ***Dosing for septic or other vasodilatory shock***

In adult patients with septic or other vasodilatory shock:

- 0,5 mcg/kg/min to 6 mcg/kg/min by intravenous continuous infusion, titrated to blood pressure goal. Doses above 6 mcg/kg/min do not show significant incremental increase in blood pressure.

## **Special populations**

### ***Patients with renal impairment***

Lower doses of RUSAINÉ may be required in patients with renal impairment.

### ***Patients with hepatic impairment***

Higher doses of RUSAINÉ may be needed in patients with liver cirrhosis.

### ***Elderly patients***

Treatment of the elderly should be made with caution.

### ***Paediatric population***

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

### **Method of administration**

For intravenous use.

RUSAINÉ should be administered by slow intravenous bolus injection or continuous intravenous infusion, after dilution.

### **4.3 Contraindications**

- Hypersensitivity to phenylephrine hydrochloride or to any of the excipients of RUSAINÉ (see section 6.1).
- Paediatric use.
- Severe uncontrolled hypertension.
- Severe hyperthyroidism.
- Severe heart-block with or without bradycardia.
- Severe uncontrolled cardiac failure.
- Severe bradycardia (less than 50 bpm).
- Seriously impaired coronary circulation.

### **4.4 Special warnings and precautions for use**

Sustained intravenous (IV) infusion may result in diminished efficacy.

Great care should be exercised in administering RUSAINÉ to patients with pre-existing cardiovascular disease, such as ischaemic heart disease, dysrhythmias, occlusive vascular disease including arteriosclerosis, hypertension or aneurysms. Increased blood pressure may occur and precipitate underlying heart failure, angina in patients with severe arteriosclerosis or past history of angina and increase pulmonary arterial pressure. Anginal pain may be precipitated in

patients with angina pectoris.

Severe bradycardia and decreased cardiac output may occur.

Excessive peripheral and visceral vasoconstriction with ischaemia to vital organs may occur, especially in patients with extensive peripheral vascular disease e.g. Raynaud's phenomenon.

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.

Care is also required when given to patients with diabetes mellitus, or closed angle glaucoma.

Avoid extravasation as this can cause necrosis or sloughing of tissue.

Use extreme caution in patients with hyperthyroidism.

Concurrent use with monoamine oxidase (MAO) inhibitors may prolong and intensify cardiac stimulation and vasopressor effects because of the release of catecholamines which accumulate in intraneuronal

storage sites during MAO inhibitor therapy; this may result in headache, cardiac dysrhythmias, vomiting or sudden and severe hypertensive or hyper-pyretic crises. For patients who have been receiving MAO inhibitors 2 to 3 weeks prior to administration of sympathomimetic medicines, the initial dosage should be reduced to be no more than one-tenth of the usual dose.

Allergic reactions, including anaphylactic symptoms, may occur in patients with sulphite-sensitivity.

Blood pressure response to RUSAINÉ may be increased in patients with autonomic dysfunction.

RUSAINÉ can increase the need for renal replacement therapy in patients with septic shock.

Monitor renal function.

***RUSAINÉ contains sodium metabisulphite***

RUSAINÉ contains sodium metabisulphite which may rarely cause severe hypersensitivity reactions and bronchospasm.

**4.5 Interaction with other medicines and other forms of interaction**

RUSAINÉ may interact with cyclopropane and halothane and other halogenated inhalational anaesthetics, to induce ventricular fibrillation. An increased risk of dysrhythmias may also occur if RUSAINÉ is given to patients receiving cardiac glycosides, quinidine, tricyclic antidepressants (e.g. imipramine) and noradrenergic-serotonergic antidepressants (venlafaxine).

RUSAINÉ is a hypertensive medicine and may consequently reverse the action of many antihypertensive medicines. The patient should be carefully monitored to confirm the desired effect is obtained.

Interactions of RUSAINÉ with alpha and beta receptor blocking medicines may be complex.

Medicines which have an effect on alpha<sub>1</sub>-adrenoceptors could potentiate (such as clonidine) or inhibit (such as doxazosin, labetalol, prazosin, haloperidol, phenothiazines) the vasopressive action of RUSAINÉ.

Concurrent use with beta-adrenergic blocking medicines (systemic or ophthalmic) may result in an exaggeration of the vasoconstriction effects and profound bradycardia.

Concomitant use of oxytocic medicines with RUSAINÉ potentiates the vasopressor-active effects. Thus, some oxytocic medicines may cause severe persistent hypertension and strokes can occur during post-partum period.

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

Severe hypertension may occur following the use of RUSAINÉ and atropine or other

antimuscarinics.

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

The cardiac stimulation and vasopressor effects of RUSAINE may be potentiated by the use of monoamine oxidase inhibitors or reversible inhibitors of monoamine oxidase, such as selegiline, moclobemide, linezolid, nialamide, pargyline, phenelzine (see section 4.4). This interaction is still possible 15 days after discontinuation of MAO inhibitor.

Concurrent use with ergot alkaloids, such as bromocriptine, lisuride, cabergoline, pergolide, dihydroergotamine, methylergometrine, methysergide and ergotamine increases the risk of vasoconstriction and/or hypertensive crisis.

Concomitant use of reserpine and other sympatholytic medicines with RUSAINE causes a 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.

#### **4.6 Fertility, pregnancy and lactation**

##### **Pregnancy**

The safety of RUSAINE during pregnancy has not been established. Due to the vasoconstrictive properties of RUSAINE, the product should be used with caution in patients with a history of pre-eclampsia. Administration of RUSAINE in late pregnancy or labour may cause foetal hypoxia and bradycardia.

##### **Breastfeeding**

The safety of RUSAINE during lactation has not been established. Excretion of phenylephrine in breast milk appears to be minimal.

## **Fertility**

There are no data available regarding fertility.

## **4.7 Effects on ability to drive and use machines**

It is not known if RUSAINÉ has an effect on the ability to drive or use machines. Caution is advised before driving a vehicle or operating machinery until the effects of RUSAINÉ are known.

## **4.8 Undesirable effects**

RUSAINÉ may cause a transient tingling and coolness of the skin and a temporary sensation of fullness in the head. Extravasation of the injection may cause local necrosis (see section 4.4).

Peripheral vasoconstriction, possibly leading to necrosis or gangrene, may occur with prolonged use of RUSAINÉ in high doses or low doses in the presence of peripheral vascular disease.

### **Immune system disorders**

*Less frequent:* hypersensitivity

*Frequency unknown:* metabolism and nutrition disorders, metabolic disorders

### **Psychiatric disorders**

*Less frequent:* anxiety, excitability, agitation, psychotic states, confusion

*Frequency unknown:* nervousness or restlessness, insomnia

### **Nervous system disorders**

*Frequent:* headache

*Less frequent:* paraesthesia, tremor

### **Eye disorders**

*Less frequent:* mydriasis, aggravation of pre-existing angle-closure glaucoma

### **Cardiac disorders**

*Less frequent:* angina pectoris, bradycardia, tachycardia, ventricular dysrhythmias

*Frequency unknown:* palpitations, cardiac arrest

### **Vascular disorders**

*Less frequent:* cerebral haemorrhage, hypertensive crisis, hypertension,  
hypotension

*Frequency unknown:* dizziness, syncope, flushing

### **Respiratory, thoracic and mediastinal disorders**

*Less frequent:* dyspnoea, pulmonary oedema

### **Gastrointestinal disorders**

*Less frequent:* nausea, vomiting

*Frequency unknown:* salivary hypersecretion

### **Skin and subcutaneous tissue disorders**

*Less frequent:* sweating, pallor or skin blanching, piloerection, skin necrosis with  
extravasation

### **Musculoskeletal and connective tissue disorders**

*Less frequent:* muscular weakness

### **Renal and urinary disorders**

*Less frequent:* difficulty in micturition, urinary retention

*Frequency unknown:* dysuria

### **General disorders and administration site conditions**

*Less frequent:* extravasation

*Frequency unknown:* infusion site necrosis, hyperhidrosis

### **Investigations**

*Frequency unknown:* abnormal blood glucose

RUSAINÉ 10 mg/mL 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 RUSAINÉ is important. It allows continued monitoring of the benefit/risk balance of RUSAINÉ. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the “**6.04 Adverse Drug Reactions**

**Reporting Form**”, found online under SAHPRA’s publications:

<https://www.sahpra.org.za/Publications/Index/8>

## **4.9 Overdose**

### ***Symptoms***

Symptoms of overdosage include headache, nausea, vomiting, palpitations, hypertension (which may be severe) and reflex bradycardia and other cardiac dysrhythmias. In severe cases confusion, hallucinations and seizures may occur.

### ***Management***

Treatment should consist of symptomatic and supportive measures. For excessive hypertensive effects, the administration should be reduced or the medication temporarily discontinued until blood pressure is

decreased. If these measures fail to lower the blood pressure, a short acting alpha-adrenergic

blocking medicine may be administered.

## **5. PHARMACOLOGICAL PROPERTIES**

### **5.1 Pharmacodynamic properties**

Category and class: A 7.2 Vasoconstrictors, pressor medicines.

Pharmacotherapeutic group: Adrenergic and dopaminergic agent.

ATC code: C01CA

Phenylephrine is an alpha 1 adrenergic receptor agonist.

Phenylephrine hydrochloride is a sympathomimetic medicine 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.

#### ***Mechanism of action***

After injection, it produces peripheral vasoconstriction and increased arterial pressure; it also causes reflex bradycardia. Beta 1 adrenergic effects are insignificant.

### **5.2 Pharmacokinetic properties**

#### **Absorption**

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 about two hours respectively. Intravenous injections are effective for up to about 20 minutes.

Following an intravenous infusion of phenylephrine hydrochloride, the effective half-life was approximately 5 minutes.

#### **Distribution**

The steady-state volume of distribution (340 L) exceeded the body volume by a factor of 5, suggesting a high distribution into certain organ compartments.

## **Biotransformation**

A mass balance study showed that phenylephrine is extensively metabolised by the liver with only 12 % of the dose excreted unchanged in the urine. Deamination by monoamino oxidase is the primary metabolic pathway resulting in the formation of the major metabolite (m-hydroxymandelic acid) which accounts for 57 % of the total administered dose.

## **Elimination**

The average total serum clearance (2095 mL/min) was close to one-third of the cardiac output.

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

Citric acid monohydrate (for pH-adjustment)

Sodium chloride

Sodium citrate dihydrate (for pH-adjustment)

Sodium metabisulphite (E223)

Water for injection.

### **6.2 Incompatibilities**

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

### **6.3 Shelf life**

2 years.

### **6.4 Special precautions for storage**

Store at or below 25 °C.

#### **6.5 Nature and contents of container**

1 mL clear Fiolax ampoule (USP Type I) with a pink OPC dot.

1 mL clear NEG ampoule (USP Type I) with a black OPC dot.

5 or 10 ampoules are placed in a plastic tray and packed in an outer carton.

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

None.

### **7. HOLDER OF CERTIFICATE OF REGISTRATION**

LeBasi Pharmaceuticals (Pty) Ltd

San Domenico Building, Unit 6, Ground Floor

10 Church Street

Durbanville

7551

### **8. REGISTRATION NUMBER**

56/7.2/0060

### **9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of registration: 06 June 2023

### **10. DATE OF REVISION OF THE TEXT**