SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

VERALAINE (Norepinephrine Bitartrate Injection USP 1mg/ml, 4ml)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:
Norepinephrine Bitartrate Injection USP
Eq. to Norepinephrine
Water for Injection USP

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Sterile Solution for injection (Injection)

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Indicated for use as an emergency measure in the restoration of blood pressure in cases of acute hypotension

4.2 Posology and method of administration

Posology
Adults
Initial rate of infusion:
When diluted as recommended (the concentration of the prepared infusion is 40 mg/litre noradrenaline base (80 mg/litre noradrenaline tartrate)) the initial rate of infusion, at a body weight of 70 kg, should be between 10 ml/hour and 20 ml/hour (0.16 to 0.33 ml/min). This is equivalent to 0.4 mg/hour to 0.8 mg/hour noradrenaline base (0.8 mg/hour to 1.6 mg/hour noradrenaline tartrate). Some clinicians may wish to start at a lower initial infusion rate of 5 ml/hour (0.08 ml/min), equivalent to 0.2 mg/hour noradrenaline base (0.4 mg/hour noradrenaline tartrate).
Titration of dose:
Once an infusion of noradrenaline has been established the dose should be titrated in steps of 0.05 -0.1 µg/kg/min of noradrenaline base according to the pressor effect observed. There is great individual variation in the dose required to attain and maintain normotension. The aim should be to establish a low normal systolic blood pressure (100 - 120 mm Hg) or to achieve an adequate mean arterial blood pressure (greater than 65 - 80 mm Hg – depending on the patient's condition)

Noradrenaline Infusion Solution 40 mg/litre (40 µg /ml) noradrenaline base			
Patient's Weight	Posology (µg/kg/min) noradrenaline base	Posology (mg/hour) noradrenaline base	Infusion Rate (ml/hour)
50 kg	0.05	0.15	3.75
	0.1	0.3	7.5
	0.25	0.75	18.75
	0.5	1.5	37.5
	1	3	75
60 kg	0.05	0.18	4.5
	0.1	0.36	9
	0.25	0.9	22.5
	0.5	1.8	45
	1	3.6	90
70 kg	0.05	0.21	5.25
	0.1	0.42	10.5

	0.25	1.05	26.25
	0.5	2.1	52.5
	1	4.2	105
80 kg	0.05	0.24	6
	0.1	0.48	12
	0.25	1.2	30
	0.5	2.4	60
	1	4.8	120
90 kg	0.05	0.27	6.75
	0.1	0.54	13.5
	0.25	1.35	33.75
	0.5	2.7	67.5
	1	5.4	135

Some clinicians may prefer to dilute to other concentrations. If dilutions other than 40 mg/l are used, check the infusion rate calculation carefully before starting treatment.

Renal or hepatic impairment:

There is no experience in the treatment of renal or hepatically impaired patients

Elderly:

As for adults

Paediatric population

Not recommended.

Duration of Treatment and Monitoring:

Noradrenaline should be continued for as long as vasoactive drug support is indicated. The patient should be monitored carefully for the duration of therapy. Blood pressure should be carefully monitored for the duration of therapy.

Withdrawal of Therapy:

The noradrenaline infusion should be gradually decreased since abrupt withdrawal can result inacute hypotension.

Route of Administration:

For intravenous use.

Method of administration:

Administer as a diluted solution via a central venous catheter.

The infusion should be at a controlled rate using either a syringe pump an infusion pump or adrip counter.

4.3. Contraindications
Hypersensitivity to noradrenaline tartrate or to any of the excipients

4.4 Special warnings and precautions for use

Noradrenaline should only be administered by healthcare professionals who are familiar with its use.
Elderly patients may be especially sensitive to the effects of noradrenaline.
Particular caution should be observed in patients with coronary, mesenteric or peripheral vascular thrombosis because noradrenaline may increase the ischemia and extend the area of infarction. Similar caution should be observed in patients with hypotension following myocardial infarction, in patients with Prinz metal's variant angina and in patients with diabetes, hypertension or hyperthyroidism.
Noradrenaline should be used with caution in patients who exhibit profound hypoxia or hypercarbia.

4.5 Interaction with other medicinal products and other forms of interaction

The use of noradrenaline with volatile halogenated anaesthetic agents, monoamine oxidase inhibitors, linezolid, tricyclic antidepressants, adrenergic-serotoninergic drugs or any other cardiac sensitizing agents is not recommended because severe, prolonged hypertension and possible arrhythmias may result.

4.6 Fertility, pregnancy, and lactation
Noradrenaline may impair placental perfusion and induce fetal bradycardia. It may also exert a contractile effect on the pregnant uterus and lead to fetal asphyxia in late pregnancy. These possible risks to the fetus should therefore be weighed against the potential benefit to the mother.
Breastfeeding
No information is available on the use of noradrenaline in lactation.

4.7 Effects on ability to drive and use machines.
Not stated.

4.8 Undesirable effects

System Organ Class	Undesirable Effect
Psychiatric disorders	Anxiety
Psychiatric disorders	Headache
Cardiac disorders	Arrhythmias (when used in conjunction with cardiac sensitising agents), bradycardia, stress cardiomyopathy
Vascular disorders	Hypertension, peripheral ischaemia including gangrene of the extremities, plasma volume depletion with prolonged use
Respiratory, thoracic and mediastinal disorders	Dyspnea
General disorders and administration site conditions	Extravasation necrosis at the injection site

Reporting of suspected adverse reactions: Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

4.9 Overdose

Overdosage may result in severe hypertension, reflex bradycardia, a marked increase in peripheral resistance and decreased cardiac output. These may be accompanied by violent headaches, photophobia, retrosternal pain, pallor, intense sweating and vomiting. In the event of overdosage, treatment should be withdrawn and appropriate corrective treatment initiated.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Adrenergic and dopaminergic agents, ATC code: C01CA03 The vascular effects in the doses normally used clinically result from the simultaneous stimulation of alpha and beta-adrenergic receptors in the heart and vascular system. Except in the heart, its action is predominantly on the alpha receptors. This results in an increase in the force (and in the absence of vagal inhibition, in the

rate) of myocardial contraction. Peripheral resistance increases and diastolic and systolic pressures are raised.
The increase in blood pressure may cause a reflex decrease in heart rate. Vasoconstriction may result in decreased blood flow in the kidneys, liver, skin and smooth muscles. Local vasoconstriction may cause haemostasis and/or necrosis.
The effect on blood pressure disappears 1-2 minutes after stopping the infusion.

5.2 Pharmacokinetic properties
Up to 16% of an intravenous dose is excreted unchanged in the urine with methylated and deaminated metabolites in free and conjugated forms.

5.3 Preclinical safety data

Most of the adverse effects attributable to sympathomimetics result from excessive stimulation of the sympathetic nervous system via the different adrenergic receptors.
Noradrenaline may impair placental perfusion and induce fetal bradycardia. It may also exert a contractile effect on the uterus and lead to fetal asphyxia in late pregnancy.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Sodium chloride
Sodium hydroxide (for pH adjustment)
Hydrochloric acid (for pH adjustment)
Water for Injections

6.2 Incompatibilities

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

Infusion solutions containing noradrenaline tartrate have been reported to be incompatible with the following substances: alkalis and oxidising agents, barbiturates, chlorpheniramine, chlorothiazide, nitrofurantoin, novobiocin, phenytoin, sodium bicarbonate, sodium iodide, streptomycin.

For compatibility with infusion bags see section 6.6.

6.3 Shelf life

18 months.

After dilution:

Chemical and physical in-use stability has been demonstrated for 24 hours at 25°C when diluted to 4 mg/litre and 40 mg/litre noradrenaline base in sodium chloride 9 mg/ml (0.9%) solution or glucose 5% solution. However, 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.

6.4 Special precautions for storage

Do not store above 25°C.
For storage conditions after dilution of the medicinal product, see section 6.3.

6.5 Nature and contents of the container

Ampoules containing 2 ml and 4 ml of concentrate.
Pack size of 5

6.6 Special precautions for disposal and other handling

Dilution instructions:

Dilute before use with glucose 5% solution or sodium chloride 9 mg/ml (0.9%) with glucose 5 % solution.

Either add 2 ml concentrate to 48 ml glucose 5% solution (or sodium chloride 9 mg/ml (0.9%) with glucose 5% solution) for administration by a syringe pump or add 20 ml of concentrate to 480 ml glucose 5 % solution (or sodium chloride 9 mg/ml (0.9%) with glucose 5% solution) for administration by drip counter. In both cases, the final concentration of the infusion solution is 40 mg/litre noradrenaline base (which is equivalent to 80 mg/litre noradrenaline tartrate). Dilutions other than 40 mg/litre noradrenaline base may also be used (see section 4.2). If dilutions other than 40 mg/litre noradrenaline base are used, check the infusion rate calculation carefully before starting treatment.
The product is compatible with PVC infusion bags.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing authorization holder and manufacturing site addresses

Marketing authorization holder:
Verve Human Care Laboratories
15-A, Pharmacity, Selaqui,
Dehradun-248011

Manufacturing site address:
Verve Human Care Laboratories
15-A, Pharmacity, Selaqui,
Dehradun-248011

Local Technical Representative:
Generics Africa Limited
Aqua Offices Suites, 5th Floor,
Murang'a Road, Nairobi, Kenya

8. Marketing authorization number
CTD10528

9. Date of first registration
28/08/2023

10. Date of revision of the text:
15/09/2023

11. Dosimetry:
Not Applicable

12. Instructions for Preparation of Radiopharmaceuticals
Not applicable