Summary of Products Characteristics

1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

METAVER (Metaraminol Bitartrate Injection USP)

1. **Strength:** 10 mg/mL

2. **Pharmaceutical form:** Sterile solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains Metaraminol Bitartrate USP Eq. to Metaraminol
Water for Injection BP

Excipients of known effects
Sodium chloride
Sodium metabisulfite
Each 1 mL of solution contains (2.26 mg) Sodium.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Sterile Solution for Injection

Description:
Glass ampoule containing a clear colourless solution having pH of 3.2 to 4.5 filled in 1.0 mlamber glass ampoule.

4. CLINICAL PARTICULARS

4.1.Therapeutic indications

For the treatment of acute hypotension due to loss of vasoconstrictor tone as may occur during spinal anaesthesia and as an adjunct to accepted remedial procedures.

4.2.Posology and method of administration

Method of Administration: For intravenous use.
Posology: Direct intravenous injection in grave emergencies: 0.5 - 5 mg (0.05 - 0.5 mL), followed by an infusion of 15 - 100 mg (1.5 - 10 mL) in 500 mL of infusion liquid.

Particular care should be taken to use the correct dose when injecting undiluted Metaraminol.

Intravenous Infusion: 15 - 100 mg (1.5 - 10.0 mL) in 500 mL Sodium Chloride Injection or Dextrose 5% Injection, adjusting the rate of infusion to maintain the blood pressure at the desired level. Higher concentrations of Metaraminol have been used when appropriate to the circumstances.

Children: Metaraminol should not be used in children under 12 years of age.

Use in the elderly: The dosage may not require modification for elderly patients; however, geriatric patients may be more sensitive to sympathomimetic agents, therefore particular caution should be taken in this age group.

4.3.Contraindications

Metaraminol Injection should not be used concurrently with cyclopropane or halothane anaesthesia, unless clinical circumstances demand it.

Metaraminol Injection is contra-indicated in patients who are hypersensitive to the active ingredient or any of the excipients used in this formulation.

There is insufficient data to recommend use in children under 12 years of age.

4.4.Special warnings and precautions for use
Caution should be exercised to avoid excessive blood-pressure changes since response to treatment with metaraminol is very variable and the ensuing control of the blood pressure may prove difficult.

Rapidly induced hypertensive responses have been reported to cause acute pulmonary oedema, cardiac arrhythmias and arrest. Metaraminol should be used with caution in patients with cirrhosis; electrolyte levels should be adequately restored if a diuresis ensues. A fatal ventricular arrhythmia was reported in a patient with Laennec's cirrhosis while receiving metaraminol tartrate. In several instances ventricular extrasystoles that appeared during infusion of metaraminol promptly subsided when the rate of flow was reduced.

With the prolonged action of metaraminol, a cumulative effect is possible. An excessive vasopressor response may cause a prolonged elevation of blood pressure, even after discontinuation of therapy. Metaraminol should be used with caution in cases of heart disease, hypertension, thyroid disease or diabetes mellitus because of the vasoconstrictor action.

Sympathomimetic amines may provoke a relapse in patients with a history of malaria.
When vasopressor amines are used for long periods, the resulting vasoconstriction may prevent adequate expansion of circulating volume and may cause perpetuation of the shock state. There is evidence that plasma volume may be reduced in all types of shock, and that the measurement of central venous pressure is useful in assessing the adequacy of the circulating blood volume. Blood, or plasma-volume expanders, should therefore be employed when the principal reason for hypotension of shock is decreased circulating volume.

In choosing the site for injection, it is important to avoid those areas generally recognised as being unsuitable for the use of any pressor agent and to discontinue the infusion immediately if infiltration or thrombosis occurs. Although the urgent nature of the patient's condition may force the choice of an unsuitable injection site, the preferred areas of injection should be used when possible. The larger veins of the antecubital fossa or thigh are preferred to the veins in the ankle or dorsum of the hand, particularly in patients with peripheral vascular disease, diabetes mellitus, Buerger's disease or conditions with coexistent hypercoagulability.

The preservative sodium metabisulfite in Metaraminol may cause hypersensitivity. In particular, it is associated with circulatory or respiratory collapse, and depression of the CNS in certain susceptible individuals, particularly in those with asthma.

Accidental spillage of Metaraminol Injection on the skin can cause dermatitic reactions linked tothe presence of the agent's preservatives.

4.5 Interaction with other medicinal products and other forms of interaction
Metaraminol should be used with caution in patients receiving digitalis, since the combination of digitalis and sympathomimetic amines is capable of causing ectopic arrhythmic activity.

Monoamine oxidase inhibitors have been reported to potentiate the action of sympathomimetic amines. The pressor effect of metaraminol is decreased but not reversed by alpha-adrenergic blocking agents.

4.6 Effects on ability to drive and use machines
No adverse effects known

7. Fertility, pregnancy and lactation

Pregnancy
There are no well-controlled studies in pregnant women. Metaraminol should be used duringpregnancy only if the potential benefit to the mother justifies the potential risk to the foetus.

Breast feeding
It is not known whether metaraminol is secreted in human milk. Because many drugs are secreted in human milk, caution should be exercised if metaraminol is given to a breastfeedingmother.

Fertility
There are no fertility data available.

4.8 Undesirable effects
The frequency of adverse events with metaraminol has not been firmly established. Excessive therapeutic effect leading to hypertension, quickly reversible by reducing the rate of infusion,and headaches are very common.

9. Overdose
Metaraminol acts rapidly. The major therapeutic effects are complete within an hour of parenteral administration. Overdosage may result in severe hypertension accompanied by headache, constricting sensation in the chest, nausea, vomiting, euphoria, diaphoresis, pulmonary oedema, tachycardia, bradycardia, sinus arrhythmia, atrial or ventricular arrhythmias, myocardialinfarction, cardiac arrest or convulsions.

If the drug has been ingested, induce emesis or perform gastric lavage. If metaraminol has been administered by subcutaneous or intramuscular injection, local ice packs may be applied to delay absorption. Intravenous infusion should be stopped immediately, but reinstated if hypotension occurs.

If needed, alpha-adrenergic blocking agents may also be useful for reducing hypertension and may have a beneficial effect on cardiac arrhythmia, if present. Parenteral diazepam may be givenfor convulsions.

5. PHARMACOLOGICAL PROPERTIES

1. Pharmacodynamic Properties

Pharmacotherapeutic group: Adrenergic and dopaminergic agent. ATC code: C01CA09. Metaraminol is a sympathomimetic agent with direct and indirect effects on adrenergic receptors. It has both alpha and beta-adrenergic activity, the former being predominant.

Metaraminol increases the force of myocardial contractions as well as having a peripheral vasoconstrictor action. It increases both systolic and diastolic blood pressures. The vasoconstrictor action of metaraminol is not affected by depletion of the tissue stores of noradrenaline. Metaraminol is highly effective in displacing and replacing noradrenaline from the stores in adrenergic neurones and competitively inhibits noradrenaline uptake. The metaraminol that is taken up by the adrenergic neurones then acts as a false transmitter.

The overall effects of metaraminol are similar to those of noradrenaline but it is much less potent and has a more prolonged action. It can cause pulmonary vasoconstriction, and pulmonary bloodpressure is elevated when cardiac output is reduced.

2. Pharmacokinetic Properties

The pressor effect of a single dose of metaraminol lasts from about 20 minutes up to one hour. Its onset is around one or two minutes after direct intravenous injection. The vasopressor effects taper off when therapy is stopped.

3. Preclinical safety data

No relevant information.

6. PHARMACEUTICAL PARTICULARS

6.1.List of excipients

Sodium Chloride, Sodium Bisulphite, Methyl paraben, Propyl paraben and Water for Injection

6.2.Incompatibilities

Metaraminol must not be mixed with the following medicinal products due to their additiveincompatibilities:

Amphotericin B Dexamethasone Prednisolone Erythromycin Hydrocortisone Methicillin Penicillin G Thiopental

6.3.Shelf life

24 months

6.4.Special precautions for storage

Store at a temperature not exceeding 30°C. Protect from light Recommended for single use only.

6.5.Nature and contents of container

Metaver Injections are supplied in amber colour glass USP Type-1 ampoule.

7. MARKETING AUTHORISATION HOLDER AND MANUFACTURING SITE ADDRESSES

Marketing Authorisation Holder

Verve Human Care Laboratories 15-A, Pharmacity,
Selaqui, Dehradun-248011, India.

Manufacturing Site:
Verve Human Care Laboratories15-A, Pharmacity,
Selaqui, Dehradun-248011, India.

8. MARKETING AUTHORISATION NUMBER
TAN 22 HM 0033

9. DATE OF FIRST REGISTRATION/RENEWAL OF THE REGISTRATION
10/01/2022

10. DATE OF REVISION OF THE TEXT