SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Metaraminol 0.5mg/ml Solution for Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 mL of solution contains 0.5 mg of metaraminol (as tartrate).

Each 10 mL ampoule contains 5 mg metaraminol.

Excipients with known effect

Sodium chloride

Sodium metabisulfite

Each 1 mL of solution contains 0.14 mmol or 3.25 mg sodium.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.

Clear colourless solution, practically free from particles.

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. Metaraminol 0.5mg/mL Solution for Injection should not be diluted before use: it is supplied ready to use.

Posology

Direct intravenous injection in grave emergencies: 0.5 - 5 mg (1 - 10 mL), which may be followed by an infusion of 15 – 100mg (30 – 200mL of metaraminol 0.5mg/mL solution for injection) titrated to clinical effect. In the event of escalating vasopressor requirement, the more concentrated metaraminol 10mg/mL solution for injection or infusion can be administered as 15 – 100mg in 500 mL of infusion liquid. When vasoactive drug support is no longer indicated, the infusion should be gradually decreased. Abrupt withdrawal can result in acute hypotension.

Paediatric population: The safety and efficacy of Metaraminol 0.5mg/mL Solution for Injection in children under 12 years of age has not been established.

No data are available.

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

Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1

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

4.4 Special warnings and precautions for use

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

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 extravasation 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 to the presence of the agent's preservatives.

Sodium content

This medicinal product contains less than 1 mmol sodium (23 mg) per mL, that is to say essentially 'sodium free'.

4.5 Interaction with other medicinal products and other forms of interaction

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

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 Fertility, pregnancy and lactation

Pregnancy

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

Breastfeeding

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 breastfeeding mother.

Fertility

There are no fertility data available.

4.7 Effects on ability to drive and use machines

Not relevant

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.

Adverse reactions listed below are classified according to frequency and system organ class (SOC). The frequencies of adverse reactions are ranked according to the following convention: Common (≥1/100 to <1/10); Uncommon (≥1/1,000 to <1/100); Rare (≥1/10,000 to <1/1,000); Very rare (<1/10,000); Not known (cannot be estimated from the available data).

System Organ Class	**Undesirable Effect**
Nervous system disorders	*Very common:* Headache
Cardiac disorders	*Not known:* Palpitations; sinus tachycardia; bradycardia; ventricular tachycardia; other cardiac arrhythmias (especially in patients with myocardial infarction); fatal ventricular arrhythmia reported in Laennec's cirrhosis.
Vascular disorders	*Very Common:* Hypertension *Not known:* Peripheral ischaemia;
Skin and Subcutaneous tissue disorders:	*Rare:* Abscess formation; tissue necrosis; sloughing.
Gastrointestinal disorders	*Not known:* Nausea.

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. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 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, myocardial infarction, 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 given for convulsions.

5 PHARMACOLOGICAL PROPERTIES

5.1 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 blood pressure is elevated when cardiac output is reduced.

5.2 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.

5.3 Preclinical safety data

No relevant information

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride

Sodium metabisulfite (E223)

Water for injections

Sodium hydroxide (for pH adjustment)

Hydrochloric acid (for pH adjustment)

6.2 Incompatibilities

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

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store below 25°C.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user and would normally not be longer than 48 hours at 2 to 8°C unless opening has taken place in controlled and validated aseptic conditions.

6.5 Nature and contents of container

10 mL clear neutral glass Type I ampoule with a red coloured spot and one-point-cut score.

Pack size: 10 ampoules in an outer carton.

6.6 Special precautions for disposal and other handling

Metaraminol 0.5 mg/mL Solution for Injection is already diluted and ready to use. It should be used without prior dilution

Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Wockhardt UK Ltd

Ash Road North, Wrexham LL13 9UF, UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 29831/0739

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

17/08/2022

10 DATE OF REVISION OF THE TEXT

13/02/2024