NEW ZEALAND DATA SHEET

1. PRODUCT NAME

Metaraminol Juno

5 mg/10 mL solution for injection.
2.5 mg/5 mL solution for injection.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

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

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection

Polypropylene pre-filled syringe containing a clear colourless solution with pH of 3.2 to 3.8.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Prevention and treatment of the acute hypotensive state occurring with spinal anaesthesia; adjunctive treatment of hypotension due to haemorrhage, reactions to medications, surgical complications, and shock associated with brain damage due to tumour or trauma.

It may also be useful as an adjunct in the treatment of hypotension due to cardiogenic shock or septicaemia.

4.2 Dose and method of administration

Metaraminol Juno may be administered by intravenous injection. Because the maximum effect is not immediately apparent, at least 10 minutes should elapse before increasing the dosage. As the effect tapers off when the vasopressor is discontinued the patient should be carefully observed so that therapy can be reinitiated promptly if the blood pressure falls too rapidly. Patients with coexistent shock and acidosis may show a poor response to vasopressors. Established methods of shock management, such as blood or fluid replacement when indicated, and other measures directed to the specific cause of the shock should also be used.

Direct Intravenous Injection
In severe shock, when time is of great importance, it may be desirable to administer metaraminol by direct intravenous injection. The suggested dose is 0.5 to 5 mg (1 to 10 mL), followed by an infusion of 15 to 100 mg in a diluent made up to a total volume of 500mL.

Metaraminol Juno is not intended for intravenous infusion. Alternative metaraminol products are available for the preparation of IV infusion.

Direct intravenous injection of undiluted solution should be employed only in instances of grave emergency when prompt action is imperative to save life. Extreme care must be exercised to give the proper dosage.

Use in one patient on one occasion only and discard any residue.

4.3 Contraindications

Use of metaraminol tartrate with cyclopropane or halothane anaesthesia should be avoided, unless clinical circumstances demand such use. Hypersensitivity to any component of this product (refer to section 6.1).

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.

Accidental spillage of Metaraminol Juno on the skin can cause dermatitic reactions linked to the presence of the product's preservatives.

Paediatric population
Metaraminol Juno injection is not recommended for use in children.

4.5 Interaction with other medicines 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 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.

Breast-feeding
It is not known whether metaraminol is secreted in human milk. Because many medicines 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

None stated.

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 suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://pophealth.my.site.com/carmreportnz/s/.

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 medicine 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.

For risk assessment and advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

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
Hydrochloric acid
Water for injections

6.2 Incompatibilities

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

Amphotericin B
Dexamethasone
Prednisolone
Erythromycin
Hydrocortisone
Methicillin
Penicillin G
Thiopental

6.3 Shelf life

24 months when stored below 25°C, do not freeze, protect from light.

<u>After dilution</u>:
Metaraminol Juno is not suitable for dilution.

6.4 Special precautions for storage

Do not store above 25°C.

Metaraminol Juno is in a ready to use pre-filled syringe.

6.5 Nature and contents of container

Sterile polypropylene pre-filled syringe of 5 or 10 mL, ready-to- use, packaged in a blister pack.

Pack size of 10 pre-filled syringes in blister packs in an outer carton.

6.6 Special precautions for disposal and other handling

Dilution instructions:
Metaraminol Juno is not suitable for dilution.

7. MEDICINE SCHEDULE

Prescription Medicine

8. SPONSOR

Juno Pharmaceutical NZ Ltd

RSM New Zealand (Auckland) Rsm House,

Level 2, 62 Highbrook Drive,

East Tamaki, Auckland, 2013, New Zealand.

For Medical Information please call 0800 816 921.

9. DATE OF FIRST APPROVAL

27 March 2020

10. DATE OF REVISION OF THE TEXT

08 April 2025

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
All	Minor Editorial changes to align with the Medsafe datasheet template
8	Update to sponsor address