Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Metaraminol 0.5mg/ ml Solution for injection in pre-filled syringe

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of solution for injection contains 0.5 mg of metaraminol (as tartrate).
Each 5 ml pre-filled syringe contains 2.5 mg of metaraminol (as tartrate).
Each 10 ml pre-filled syringe contains 5 mg of metaraminol (as tartrate).

Excipient with known effect: sodium
Each ml of solution for injection contains 3.5 mg equivalent to 0.15 mmol of sodium.
Each 5 ml pre-filled syringe contains 17.7 mg equivalent to 0.77 mmol of sodium.
Each 10 ml pre-filled syringe contains 35.4 mg equivalent to 1.54 mmol of sodium.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection in pre-filled syringe (Injection)
Clear, colourless liquid.
pH: 3.2 to 3.8.
Osmolality: 270-330 mOsm/kg.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Metaraminol 0.5 mg/ml solution for injection in pre-filled syringe is indicated 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 in adults.

4.2 Posology and method of administration

Posology

Metaraminol 0.5 mg/ml solution for injection in pre-filled syringe should only be administered by healthcare professionals with appropriate training and relevant experience. The dose of metaraminol should be carefully adapted according to official current guidelines.

Adults
Direct intravenous injection in grave emergencies: 0.5 to 5 mg (1 to 10 ml).
One direct IV injection should usually not exceed 1 mg.
The maximum cumulative dose after repeated direct intravenous injections is 5 mg.

Metaraminol 0.5 mg/ml solution for injection in pre-filled syringe is not suitable for intravenous infusion.

Paediatric population
The safety and efficacy of this medicine in children and adolescents have not been established. There are insufficient data to support its use in this population.

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.

Method of administration

For intravenous use.
Metaraminol 0.5 mg/ml solution for injection should not be diluted before use: it is supplied ready to use in pre-filled syringes. The pre-filled syringe is not suitable for syringe pump drivers.

4.3 Contraindications

Metaraminol, solution for injection in pre-filled syringe should not be used concurrently with cyclopropane or halothane anaesthesia, unless clinical circumstances demand it (see section 4.5).

Metaraminol, solution for injection in pre-filled syringe is contra-indicated in patients who are hypersensitive to the active ingredient or any of the excipients listed in 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. 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.

In case of extravasation, local administration of an alpha blocker such as phentolamine may prevent the risk of necrosis.
Metaraminol, solution for injection in pre-filled syringe is to be used by direct intravenous injection only. Bolus doses should be administered at the minimal efficient dose. Metaraminol should be administered under comprehensive hemodynamic monitoring.

Excipients
This medicinal product contains less than 1 mmol sodium (23 mg) per 5 ml syringe, that is to say essentially "sodium free".
This medicinal product contains 35.4 mg sodium per 10 ml syringe, equivalent to 1.8 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.

4.5 Interaction with other medicinal products and other forms of interaction

Metaraminol, solution for injection in pre-filled syringe should not be used concurrently with cyclopropane or halothane anaesthesia, unless clinical circumstances demand it, due to a risk of serious venticular arrhythmia (see section 4.3).

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.

A close monitoring of blood pressure is recommended in case of co-administration with oxytocic medicines due to the risk of enhancement of metaraminol effects.

In case of co-administration of metaraminol and ergot alkaloids, there is a risk of vasoconstriction and/or hypertensive crisis.

Co-administration with tricyclic antidepressants may enhance the effect of metaraminol.

Co-administration with doxapram may enhance the effect of metaraminol.

Co-administration with guanethidine may alter the effects of both medications.

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 fetus.

Breastfeeding
It is not known whether metaraminol is 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: Very Common (≥1/10); 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).

	Very common (≥1/10)	**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)**
Psychiatric disorders						Anxiety, fear, confusion, irritability, psychotic state
Nervous system disorders	Headache					Restlessness, dizziness, insomnia
Cardiac disorders						Palpitations; sinus or ventricular tachycardia; bradycardia; other cardiac arrhythmias (especially in patients with myocardial infarction); fatal ventricular arrhythmia reported in Laennec's

						cirrhosis
Vascular disorders	Hypertension					Flushing, rebound hypotension, peripheral ischaemia
Gastrointestinal disorders						Nausea, vomiting
Renal and urinary disorders						Difficulty in micturition, urinary retention
General disorders and administration site conditions				Abscess formation; tissue necrosis; sloughing		Sweating

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 HPRA Pharmacovigilance - Website: www.hpra.ie

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, convulsions or cerebral haemorrhage.

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.

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

Absorption

Metaraminol, when administered as an intravenous bolus in doses ranging from 0.5 to 5 mg, has a rapid onset of action within 1–2 minutes. Its peak effect occurs at around 10 minutes, and the duration of action lasts between 20 and 60 minutes.

Distribution
The active substance accumulates in organs rich in norepinephrine storage vesicles, such as the heart, spleen, and adrenal glands. Notably, metaraminol does not cross the blood-brain barrier.

Metabolism
Approximately 45% of metaraminol is bound to plasma proteins. It undergoes hepatic metabolism, indicating the liver plays a significant role in its biotransformation.

Elimination
Metaraminol is primarily excreted through the kidneys and bile, mostly in the form of metabolites. However, it remains unclear whether these metabolites retain pharmacological activity.

5.3 Preclinical safety data

No relevant information.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Chloride
Hydrochloric acid (pH adjustment)
Water for injections

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Unopened blister pack:2 years
After opening, the medicinal product should be used immediately.

6.4 Special precautions for storage

Keep the pre-filled syringe in its unopened blister until use.
Do not freeze.

6.5 Nature and contents of container

5 ml or 10 ml solution for injection in a polypropylene pre-filled syringe with a chlorobutyl plunger stopper, individually packaged in a transparent blister.
Cardboard box of 10 pre-filled syringes.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

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

Instructions for use:
Metaraminol 0.5 mg/ml solution for injection is already diluted and ready to use in pre-filled syringes. It should be used without prior dilution.

Please prepare the syringe carefully as follows

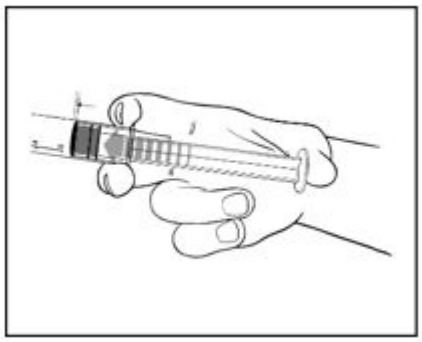
The pre-filled syringe is for single use only. Discard the pre-filled syringe after use. DO NOT REUSE.

The content of an un-opened and un-damaged blister is sterile, and the blister must not be opened until the syringe is ready to be used.
The product should be inspected visually for particles and discoloration prior to administration. Only a clear colourless solution free from particles or precipitates should be used.
The product should not be used if the tamper-evident seal on the syringe is broken.

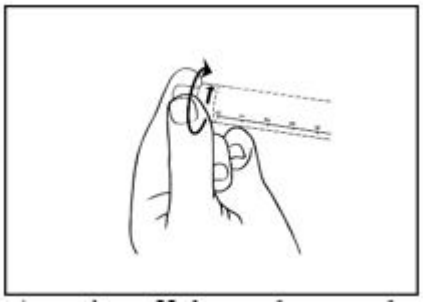
The external surface of the syringe is sterile until the blister is opened.

When handled using an aseptic method, the syringe can be placed on a sterile field.

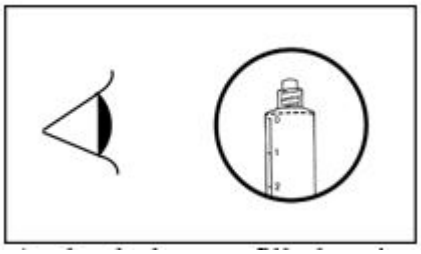
1) Withdraw the pre-filled syringe from the sterile blister.



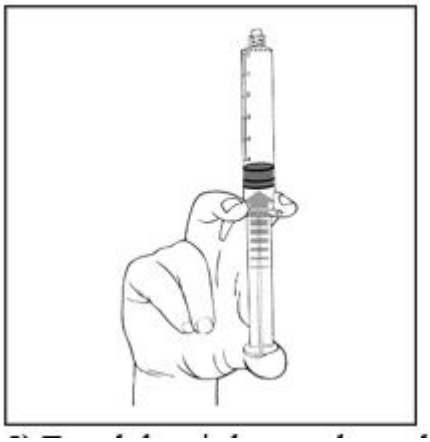
2) Push on the plunger to free the bung. The sterilisation process may have caused adhesion of the bung to the body of the syringe.



3) Twist off the end cap to break the seal. Do not touch the exposed luer connection in order to avoid contamination.



4) Check the pre-filled syringe seal tip has been completely removed. If not, replace the cap and twist again



5) Expel the air by gently pushing the plunger.

6) Connect the pre-filled syringe to the IV access. Push the plunger slowly to inject the required volume.

7 MARKETING AUTHORISATION HOLDER

Laboratoire Aguettant
1 Rue Alexander Fleming
Lyon
69007
France

8 MARKETING AUTHORISATION NUMBER

PA1968/024/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of 1st authorisation: 18th September 2026

10 DATE OF REVISION OF THE TEXT