Metaraminol Bitartrate injection

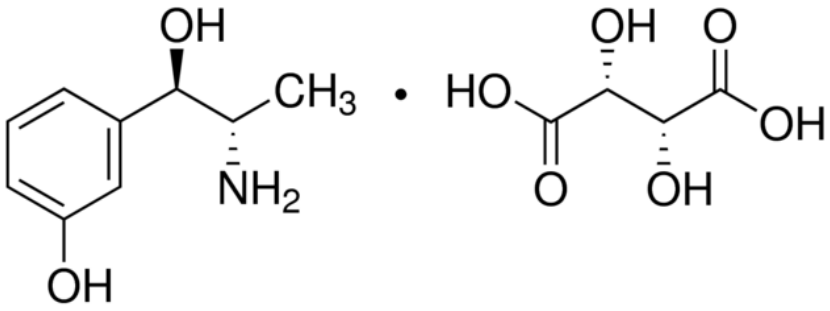
The incidence of anaphylactic reactions associated with anesthesia is difficult to predict, but it is estimated that a suspected anaphylactic reaction occurs in 1 in 3500 anesthetics, with a true anaphylaxis seen in 1 in 6000. The most commonly responsible are neuromuscular blocking agents, latex, antibiotics and aesthetics (like Propofol or Sevoflurane). Currently available anesthetics can cause large falls in blood pressure.

There are no guidelines or algorithms for management of anaphylaxis that include the use of vasopressor other than epinephrine; however, there are many documented and reported cases of ineffectiveness of epinephrine. In such cases return of spontaneous circulation was achieved with the administration of metaraminol.

Description

Metaraminol bitartrate is a potent sympathomimetic amine that increases both systolic and diastolic blood pressure.

Metaraminol bitartrate is:
[*R* -(*R* *, *S* *)] -(alpha) -(1-aminoethyl)-3-hydroxybenzenemethanol [*R* -(*R* *, R *)]-2,3-dihydroxybutanedioate (1:1) (salt), which is levorotatory.
Its empirical formula is $C_9 H_{13} NO_2 \cdot C_4 H_6 O_6$ and its structural formula is:



Metaraminol bitartrate is a white, crystalline powder with a molecular weight of 317.29, is freely soluble in water, slightly soluble in alcohol, and practically insoluble in chloroform and in ether.

Metaraminole Injection

Metaraminol Bitartrate injection is a “generic medicine”. This means that Metaraminole Injection is similar to a “reference medicine” already authorized in several countries, as for example UK and USA, with the brand name of ARAMINE 10mg/ml solution for injection (PL 00025/5020R in UK from Merck, Sharp & Dome Limited) which was granted a full Marketing Authorization on 14 June 1989 and a Product License on 26 February 1973.

The Product License for Aramine 10mg/ml solution for injection was cancelled on the 02 April 2009 and is not marketed in the European Union.

Metaraminol 10mg/ml solution for injection or infusion contains the active ingredient metaraminol bitartrate, a sympathomimetic agent which falls into adrenergic and dopaminergic pharmaco-therapeutic group.

Quality and composition

Metaraminole injection is a sterile solution.

Each mL contains:

- Metaraminol bitartrate equivalent to metaraminol 10 mg

Inactive ingredients:

- Sodium chloride
- Sodium meta-bisulfite
- Water for Injection

The finished product is supplied in glass ampoules containing 1ml of a clear solution for injection or infusion, in a pack size of 5 or 10 ampoules per pack, packaged in cartons.

Clinical Pharmacology

The pressor effect of Metaraminol Bitartrate begins in 1 to 2 minutes after intravenous infusion, in about 10 minutes after intramuscular injection, and in 5 to 20 minutes after subcutaneous injection. The effect lasts from about 20 minutes to one hour. METARAMINOL BITARTRATE has a positive inotropic effect on the heart and a peripheral vasoconstrictor action.

Renal, coronary, and cerebral blood flow are a function of perfusion pressure and regional resistance. In patients with insufficient or failing vasoconstriction, there is additional advantage to the peripheral action of METARAMINOL BITARTRATE, but in most patients with shock, vasoconstriction is adequate and any further increase is unnecessary. Blood flow to vital organs may decrease with METARAMINOL BITARTRATE if regional resistance increases excessively.

The pressor effect of METARAMINOL BITARTRATE is decreased but not reversed by alpha-adrenergic blocking agents. Primary or secondary fall in blood pressure and tachyphylaxis response to repeated use are uncommon.

Indications and Usage

METARAMINOL BITARTRATE is indicated for prevention and treatment of the acute hypotensive state occurring with spinal anesthesia. It is also indicated as adjunctive treatment of hypotension due to hemorrhage, reactions to medications, surgical complications, and shock associated with brain damage due to trauma or tumor.

Contraindications

Use of METARAMINOL BITARTRATE with cyclopropane or halothane anesthesia should be avoided, unless clinical circumstances demand such use.

Hypersensitivity to any component of this product, including sulfites.

Warnings

Use of sympathomimetic amines with monoamine oxidase inhibitors or tricyclic antidepressants may result in potentiation of the pressor effect.

METARAMINOL BITARTRATE contains sodium meta-bisulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in no asthmatic people.

Precautions

General

Caution should be used to avoid excessive blood pressure response. Rapidly induced hypertensive responses have been reported to cause acute pulmonary edema, arrhythmias, cerebral hemorrhage, or cardiac arrest.

Patients with cirrhosis should be treated with caution, with adequate restoration of electrolytes if diuresis ensues. Fatal ventricular arrhythmia was reported in one patient with Laennec's cirrhosis while receiving metaraminol bitartrate. In several instances, ventricular extra systoles that appeared during infusion of this vasopressor subsided promptly when the rate of infusion was reduced.

With the prolonged action of METARAMINOL BITARTRATE, a cumulative effect is possible. If there is an excessive vasopressor response there may be a prolonged elevation of blood pressure even after discontinuation of therapy.

When vasopressor amines are used for long periods, the resulting vasoconstriction may prevent adequate expansion of circulating volume and may cause perpetuation of shock. 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. Therefore, blood or plasma volume expanders should be used when the principal reason for hypotension or shock is decreased circulating volume.

Because of its vasoconstrictor effect, METARAMINOL BITARTRATE should be given with caution in heart or thyroid disease, hypertension, or diabetes. Sympathomimetic amines may provoke a relapse in patients with a history of malaria.

Drug Interactions

METARAMINOL BITARTRATE should be used with caution in digitalized patients, since the combination of digitalis and sympathomimetic amines may cause ectopic arrhythmias.

Monoamine oxidase inhibitors or tricyclic antidepressants may potentiate the action of sympathomimetic amines. Therefore, when initiating pressor therapy in patients receiving these drugs, the initial dose should be small and given with caution.

Carcinogenesis, Mutagenesis,

Impairment of Fertility

Studies in animals have not been performed to evaluate the mutagenic or carcinogenic potential of METARAMINOL BITARTRATE or its potential to affect fertility.

Pregnancy

Pregnancy Category C. Animal reproduction studies have not been conducted with METARAMINOL BITARTRATE. It is not known whether METARAMINOL BITARTRATE can cause fetal harm when given to a pregnant woman or can affect reproduction capacity. METARAMINOL BITARTRATE should be given to a pregnant woman only if clearly needed.

Nursing Mothers

It is not known whether this drug is secreted in human milk. Because many drugs are secreted in human milk, caution should be exercised when METARAMINOL BITARTRATE is given to a nursing woman.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

Adverse Reactions

Sympathomimetic amines, including METARAMINOL BITARTRATE, may cause sinus or ventricular tachycardia, or other arrhythmias, especially in patients with myocardial infarction.

In patients with a history of malaria, these compounds may provoke a relapse.

Abscess formation, tissue necrosis, or sloughing rarely may follow the use of METARAMINOL BITARTRATE. In choosing the site of injection, it is important to avoid those areas recognized as *not* suitable for use of any pressor agent and to discontinue the infusion immediately if infiltration or thrombosis occurs. Although the physician may be forced by the urgent nature of the patient's condition to choose injection sites that are not recognized as suitable, he should, when possible, use the preferred areas of injection. The larger veins of the antecubital fossa or the thigh are preferred to veins in the dorsum of the hand or ankle veins, particularly in patients with peripheral vascular disease, diabetes mellitus, Buerger's disease, or conditions with coexistent hypercoagulability.

Overdosage

Overdosage may result in severe hypertension accompanied by headache, constricting sensation in the chest, nausea, vomiting, euphoria, diaphoresis, pulmonary edema, tachycardia, bradycardia, sinus arrhythmia, atrial or ventricular arrhythmias, cerebral hemorrhage, myocardial infarction, cardiac arrest or convulsions.

Should an excessive elevation of blood pressure occur, it may be immediately relieved by a sympatholytic agent, e.g., phentolamine. An appropriate antiarrhythmic agent may also be required.

The oral LD_{50} in the rat and mouse is 240 mg/kg and 99 mg/kg, respectively.

Dosage and Administration

METARAMINOL BITARTRATE may be given intramuscularly, subcutaneously, or intravenously, the route depending on the nature and severity of the indication.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to use, whenever solution and container permit.

Allow at least 10 minutes to elapse before increasing the dose because the maximum effect is not immediately apparent. When the vasopressor is discontinued, observe the patient carefully as the effect of the drug tapers off, so that therapy can be reinitiated promptly if the blood pressure falls too rapidly. The response to vasopressors may be poor in patients with coexistent shock and acidosis. When indicated, established methods of shock management should be used, such as blood or fluid replacement.

Intramuscular or Subcutaneous Injection. The recommended dose is 2 to 10 mg (0.2 to 1 mL). As with other agents given subcutaneously, only the preferred sites of injection, as set forth in standard texts, should be used.

Intravenous Infusion. The recommended dose is 15 to 100 mg (1.5 to 10 mL) in 500 mL of Sodium Chloride Injection or 5% Dextrose Injection, adjusting the rate of infusion to maintain the blood pressure at the desired level. Higher concentrations of METARAMINOL BITARTRATE, 150 to 500 mg per 500 mL of infusion fluid, have been used.

If the patient needs more saline or dextrose solution at a rate of flow that would provide an excessive dose of the vasopressor, the recommended volume of infusion fluid (500 mL) should be increased accordingly. METARAMINOL BITARTRATE may also be added to *less* than 500 mL of infusion fluid if a smaller volume is desired.

Compatibility Information

In addition to Sodium Chloride Injection and Dextrose Injection 5%, the following infusion solutions were found physically and chemically compatible with Injection METARAMINOL BITARTRATE when 5 mL of Injection METARAMINOL BITARTRATE, 10 mg/mL (metaraminol equivalent), was added to 500 mL of infusion solution: Ringer's Injection, Lactated Ringer's Injection, Dextran 6% in Saline , Normosol-R pH 7.4 , and Normosol-M in D5-W .

When Injection METARAMINOL BITARTRATE is mixed with an infusion solution, sterile precautions should be observed. Since infusion solutions generally do not contain preservatives, mixtures should be used within 24 hours.

Direct Intravenous Injection: In severe shock, when time is of great importance, this agent should be given by direct intravenous injection. The suggested dose is 0.5 to 5 mg (0.05 to 0.5 mL), followed by an infusion of 15 to 100 mg (1.5 to 10 mL) in 500 mL of infusion fluid as described previously.

Ampoules are sterilized by aseptic filtration, aseptically filled and then they can be sterilized by autoclaving.

How Supplied

Injection METARAMINOL BITARTRATE, containing metaraminol bitartrate equivalent to 10 mg of metaraminol per mL, is a clear, colorless solution and is supplied as follows:

- glass ampoules containing 1ml of a clear solution for injection or infusion, in a pack size of 5 or 10 ampoules per pack, packaged in cartons

Storage

Store at 25°C (77°F); excursions permitted to 15-30°C(59-86°F) [see USP Controlled Room Temperature]. Store container in carton until contents have been used. Protect from light. Protect from freezing.

What is Metaraminol Bitartrate?

Metaraminol Bitartrate Injectable is used for Hypotension, Priapism and other conditions. Metaraminol Bitartrate Injectable may also be used for purposes not listed in this medication guide.
Metaraminol Bitartrate Injectable contains Metaraminol Bitartrate as an active ingredient.
Metaraminol Bitartrate Injectable works by increasing the pumping action of the heart and by narrowing the blood vessels.

Detailed information related to Metaraminol Bitartrate Injectable's uses, composition, dosage, side effects and reviews is listed below

Metaraminol Bitartrate Injectable Uses

Metaraminol Bitartrate Injectable is used for the treatment, control, prevention, & improvement of the following diseases, conditions and symptoms:

- Hypotension
- Priapism
- Metaraminol Bitartrate Injectable may also be used for purposes not listed here.

Metaraminol Bitartrate Injectable Working, Mechanism of Action and Pharmacology

Metaraminol Bitartrate Injectable improves the patient's condition by performing the following functions:

- Increasing the pumping action of the heart and by narrowing the blood vessels.

Metaraminol Bitartrate Injectable - Composition and Active Ingredients

Metaraminol Bitartrate Injectable is composed of the following active ingredients (salts)

- Metaraminol Bitartrate

Please note that this medicine may be available in various strengths for each active ingredient listed above.

Metaraminol Bitartrate Injectable - Side-effects

The following is a list of possible side-effects that may occur from all constituting ingredients of Metaraminol Bitartrate Injectable. This is not a comprehensive list. These side-effects are possible, but do not always occur. Some of the side-effects may be rare but serious. Consult your doctor if you observe any of the following side-effects, especially if they do not go away.

- Hypertension
- Cerebral hemorrhage
- Convulsions
- Pulmonary edema
- Cardiac arrest
- Arrhythmias
- Metaraminol Bitartrate Injectable may also cause side-effects not listed here.

If you notice other side-effects not listed above, contact your doctor for medical advice. You may also report side-effects to your local food and drug administration authority

Metaraminol Bitartrate Injectable - Precautions & How to Use

Before using Metaraminol Bitartrate Injectable, inform your doctor about your current list of medications, over the counter products (e.g. vitamins, herbal supplements, etc.), allergies, pre-existing diseases, and current health conditions (e.g. pregnancy, upcoming surgery, etc.). Some health conditions may make you more susceptible to the side-effects of the drug. Take as directed by your doctor or follow the direction printed on the product insert. Dosage is based on your condition. Tell your doctor if your condition persists or worsens. Important counseling points are listed below.

- go for close electrocardiographic monitoring during treatment

Metaraminol Bitartrate Injectable - Drug Interactions

If you use other drugs or over the counter products at the same time, the effects of Metaraminol Bitartrate Injectable may change. This may increase your risk for side-effects or cause your drug not to work properly. Tell your doctor about all the drugs, vitamins, and herbal supplements you are using, so that you doctor can help you prevent or manage drug interactions. Metaraminol Bitartrate Injectable may interact with the following drugs and products:

- Chloroform
- Cocaine
- Diuretics
- Doxazosin
- Ergonovine
- Monoamine oxidase inhibitors