1 PRODUCT NAME

Ephedrine Hydrochloride Injection 30mg/ml, solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Ephedrine hydrochloride 30mg/ml

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Clear, colourless solution for Injection

pH = 5.00 – 7.000

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Ephedrine Hydrochloride Injection is indicated in the treatment of hypotension secondary to spinal anaesthesia.

4.2 Dose and method of administration

Ephedrine Hydrochloride Injection is administered by the intravenous route.

Adults and Elderly

Ephedrine hydrochloride should be administered in the lowest effective dose.
A 3 mg/mL solution should be given as a slow intravenous injection of 3 to 7.5 mg (maximum 10 mg), repeated as needed every 3 - 4 minutes to a maximum of 30 mg.
A lack of efficacy after 30 mg should lead to reconsideration of the choice of therapeutic agent.

Children

Ephedrine hydrochloride injection is not approved for use in this patient population.

4.3 Contraindications

Hypersensitivity to Ephedrine hydrochloride or to any of the excipients listed in section 6.1.

- In combination with other indirect sympathomimetic agents such as phenylpropanolamine, phenylephrine, pseudoephedrine and methylphenidate.
- In combination with alpha sympathomimetic agents.
- In combination with non-selective Monoamine Oxidase Inhibitors (MAOI) or within 14 days of their withdrawal.

4.4 Special warnings and precautions for use

Ephedrine should be used with caution in patients who may be particularly susceptible to their effects, particularly those with hyperthyroidism. Great care is also needed in patients with

cardiovascular disease such as ischaemic heart disease, arrhythmia or tachycardia, occlusive vascular disorders including arteriosclerosis, hypertension, or aneurysms. Angina pain may be precipitated in patients with angina pectoris.

Care is also required when Ephedrine is given to patients with diabetes mellitus, closed-angle glaucoma or prostatic hypertrophy.

Ephedrine should be avoided or used with caution in patients undergoing anaesthesia with cyclopropane, halothane, or other halogenated anaesthetics, as they may induce ventricular fibrillation. An increased risk of arrhythmias may also occur if Ephedrine is given to patients receiving cardiac glycosides, quinidine, or tricyclic antidepressants.

Many sympathomimetics interact with monoamine oxidase inhibitors, and should not be given to patients receiving such treatment or within 14 days of its termination. It is advisable to avoid sympathomimetics when taking reversible MAO inhibitors.

Ephedrine increases blood pressure and therefore special care is advisable in patients receiving antihypertensive therapy. Interactions of Ephedrine with alpha- and beta-blocking drugs may be complex. Propranolol and other beta-adrenoceptor blocking agents antagonise the effects of $beta_2$ adrenoceptor stimulants ($beta_2$ agonists) such as salbutamol.

Adverse metabolic effects of high doses of $beta_2$ agonists may be exacerbated by concomitant administration of high doses of corticosteroids; patients should therefore be monitored carefully when the two forms of therapy are used together although this precaution is not so applicable to inhaled corticotherapy.

Hypokalaemia associated with high doses of $beta_2$ agonists may result in increased susceptibility to digitalis-induced cardiac arrhythmias.

Hypokalaemia may be enhanced by concomitant administration of aminophylline or other xanthines, corticosteroids, or by diuretic therapy.

Precautions for use

Ephedrine should be used with caution in patients with a history of cardiac disease.

Athletes should be informed that this preparation contains an active substance which might give a positive reaction in anti-doping tests.

Check that the solution is clear and contains no visible particles before infusion.

4.5 Interaction with other medicines and other forms of interaction

Contraindicated combinations:

Indirect sympathomimetic agents (phenylpropanolamine, pseudoephedrine, phenylephrine, methylphenidate)

Risk of vasoconstriction and/or of acute episodes of hypertension.

Alpha sympathomimetics (oral and/or nasal route of administration)

Risk of vasoconstriction and/or episodes of hypertension.

Non-selective MAO inhibitors

Paroxysmal hypertension, hyperthermia possibly fatal.

Combinations not recommended:

Ergot alkaloids (dopaminergic action)

Risk of vasoconstriction and/or episodes of hypertension.

Ergot alkaloids (vasoconstrictors)

Risk of vasoconstriction and/or episodes of hypertension.

Selective MAO-A inhibitors (administered concomitantly or within the last 2 weeks)

Risk of vasoconstriction and/or episodes of hypertension.

Linezolid

Risk of vasoconstriction and/or episodes of hypertension

Tricyclic antidepressants (e.g. imipramine)

Paroxysmal hypertension with possibility of arrhythmias (inhibition of adrenaline or noradrenaline entry in sympathetic fibres).

Noradrenergic-serotoninergic antidepressants (minalcipran, venlafaxine)

Paroxysmal hypertension with possibility of arrhythmias (inhibition of adrenaline or noradrenaline entry in sympathetic fibres).

Guanethidine and related products

Substantial increase in blood pressure (hyper reactivity linked to the reduction in sympathetic tone and/or to the inhibition of adrenaline or noradrenaline entry in sympathetic fibres).

If the combination cannot be avoided, use with caution lower doses of sympathomimetic agents.

Sibutramine

Paroxysmal hypertension with possibility of arrhythmia (inhibition of adrenaline or noradrenaline entry in sympathetic fibres).

Halogenated volatile anaesthetics

Risk of perioperative hypertensive crisis and serious ventricular arrhythmias.

Combinations requiring precautions for use:

Theophylline

Concomitant administration of ephedrine and theophylline may result in insomnia, nervousness and gastrointestinal complaints.

Corticosteroids

Ephedrine has been shown to increase the clearance of dexamethasone.

Antiepileptics

Increased plasma concentration of phenytoin and possibly of phenobarbitone and primidone.

Doxapram

Risk of hypertension.

Oxytocin

Hypertension with vasoconstrictor sympathomimetics.

Hypotensive agents

Reserpine and methyldopa may reduce the vasopressor action of ephedrine.

4.6 Fertility, pregnancy and lactation

Pregnancy

Studies in animals have shown a teratogenic effect.

Clinical data from epidemiological studies on a limited number of women appear to indicate no particular effects of ephedrine with respect to malformation.

Isolated cases of maternal hypertension have been described after abuse or prolonged use of vasoconstrictor amines.

Ephedrine crosses the placenta and this has been associated with an increase in foetal heart rate and beat-to-beat variability.

Therefore, ephedrine should be avoided or used with caution, and only if necessary, during pregnancy.

Breast-feeding

Ephedrine is excreted in breast milk. Irritability and disturbed sleep patterns have been reported in breast-fed infants. There is evidence that ephedrine is eliminated within 21 to 42 hours after administration, therefore a decision needs to be made on whether to avoid ephedrine therapy or lactation should be suspended for 2 days following its administration taking into account the benefit of breastfeeding for the child and the benefit of therapy for the woman.

Fertility

The effects of ephedrine hydrochloride on male and female fertility have not been investigated in animal studies.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

Very common: ≥1/10; Common: ≥1/100, <1/10; Uncommon: ≥1/1,000, <1/100; Rare: ≥1/10,000, <1/1,000; Very rare: <1/10,000; Not known: cannot be estimated from the available data

Blood and lymphatic system disorders:

Not known: primary haemostasis modifications

Immune system disorders:

Not known: hypersensitivity

Psychiatric disorders:

Common: confusion, anxiety, depression

Not known: psychotic states, fear

Nervous system disorders:

Common: nervousness, irritability, restlessness, weakness, insomnia, headache, sweating

Not known: tremor, hypersalivation

Eye disorders:

Not known: episodes of angle-closure glaucoma

Cardiac disorders:

Common: palpitations, hypertension, tachycardia

Rare: cardiac arrhythmias

Not known: angina pain, reflex bradycardia, cardiac arrest, hypotension

Vascular disorders:

Not known: cerebral haemorrhage

Respiratory, thoracic and mediastinal disorders:

Common: dyspnoea

Not known: pulmonary oedema

Gastrointestinal disorders:

Common: nausea, vomiting

Not known: reduced appetite

Renal and urinary disorders:

Rare: acute urinary retention

Investigations:

Not known: hypokalaemia, changes in blood glucose levels

Reporting of suspected adverse reactions

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://nzphvc.otago.ac.nz/reporting/

4.9 Overdose

Symptoms

In the event of overdose, the occurrence of nausea, vomiting, fever, paranoid psychosis, ventricular and supraventricular arrhythmias, hypertension, respiratory depression, convulsions and coma are observed.

The lethal dose in humans is approximately 2 g corresponding to blood concentrations of approximately 3.5 to 20 mg/l.

Treatment

The treatment of ephedrine overdose with this product may require intensive supportive treatment. Slow intravenous injection of labetalol 50 - 200 mg may be given with electrocardiograph monitoring for the treatment of supraventricular tachycardia. Marked hypokalaemia (< 2.8 $mmol.l^{-1}$) due to compartmental shift of potassium predisposes to cardiac arrhythmias and may be corrected by infusing potassium chloride in addition to propranolol and correcting respiratory alkalosis, when present.

A benzodiazepine and/or a neuroleptic agent may be required to control CNS stimulant effects.

For severe hypertension, parenteral antihypertensive options include intravenous nitrates, calcium channel blockers, sodium nitroprusside, labetalol or phentolamine. The choice of antihypertensive drug is dependent on availability, concomitant conditions and the clinical status of the patient.

For 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 & Dopaminergic Agent, ATC Code: C01CA26

Ephedrine is a sympathomimetic amine acting directly on the alpha and beta receptors and indirectly by increasing the release of noradrenaline by the sympathetic nerve endings. As with any sympathomimetic agent, ephedrine stimulates the central nervous system, the cardiovascular system, the respiratory system, and the sphincters of the digestive and urinary systems. Ephedrine is also a monoamine oxidase (MAO) inhibitor.

5.2 Pharmacokinetic properties

After intravenous administration, ephedrine is completely biologically available, and after oral administration, the bioavailability of ephedrine has been reported to be above 90%.

Excretion depends on urine pH:

From 73 to 99% (mean: 88%) in acidic urine,

From 22 to 35% (mean: 27%) in alkaline urine.

After oral or parenteral administration, 77% of ephedrine is excreted in unchanged form in the urine.

The half-life depends on urine pH. When the urine is acidified at pH = 5, the half-life is 3 hours; when the urine is rendered alkaline at pH = 6.3, the half-life is approximately 6 hours.

5.3 Preclinical safety data

There is no pre-clinical data of relevance to the prescriber which is additional to that already included in other sections of the data sheet.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for injections

6.2 Incompatibilities

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

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store at or below 25°C. Keep in the outer carton.

6.5 Nature and contents of container

1 ml in type I colourless neutral glass ampoules. Fusion sealed. Packed into cartons of 10 ampoules.

6.6 Special precautions for disposal and other handling

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

7 MEDICINE SCHEDULE

Class B2 Controlled Drug

8 SPONSOR

Max Health Ltd, P O Box 65 231, Mairangi Bay, Auckland 0754

Ph:(09) 815 2664.

9 DATE OF FIRST APPROVAL

22 March 2012

10 DATE OF REVISION OF THE TEXT

21 December 2020

SUMMARY TABLE OF CHANGES

Date of Revision	Section Changed	Summary of new information
15 March 2018	All	• New data sheet. Incorrect source used for original data sheet. SPC format.
21 December 2020	4.1	• Correction