pharmaniaga®

Ephedrine Hydrochloride 30mg/mL Injection

COMPOSITION
Each mL contains Ephedrine Hydrochloride 30mg.

PRODUCT DESCRIPTION
A colourless to pale yellow solution.

Pharmaniaga Ephedrine Hydrochloride 30mg/ml Injection is compatible with the following infusion solutions:

- Sodium Chloride 9mg/ml (0.9%)
- Ringer's Lactate Solution
- Glucose 50mg/ml (5%)

The solution should be clear, colourless solution when diluted. After dilution, the solution must be used within 72 hours at temperature below 30°C and up to 24 hours at temperature 2-8°C after diluted with the compatible solutions listed above.

PHARMACODYNAMICS
Ephedrine is a sympathomimetic agent with direct and indirect effects on adrenergic receptors. It has alpha and beta adrenergic activity and has pronounced stimulating effects on the CNS, with a more prolonged but less potent action than adrenaline, producing peripheral vasoconstriction and raised blood pressure, bronchodilatation, reduced intestinal tone and motility, relaxation of bladder wall with contraction of sphincter muscle. It relaxes the detrusor muscle of the bladder and contracts the uterus. It has a stimulant action on the respiratory centre

PHARMACOKINETICS
Readily absorbed after oral or percutaneous administration. Effective bronchodilator plasma concentrations are in the range of 35-80 ng/mL. Plasma half-life, 3-11 hours. Accumulates in the liver, lungs, kidneys, spleen and brain. Metabolic reactions: N-Demethylation and oxidative deamination followed by conjugation.

Excretion: Up to about 95% of a dose may be excreted in the urine in 24 hours, 55-75 % as unchanged drug, 8-20% as the N-demethylated metabolite and 6-13% as deaminated metabolites such as benzoic acid, hippuric acid and 1-phenyl-propane-1,2-diol; the rate of urinary excretion of ephedrine is pH-dependent and is increased in acid urine.

INDICATION
Treatment of bronchial spasm in asthma, adjunct to correct haemodynamic imbalances and treat hypotension in epidural and spinal anaesthesia.

RECOMMENDED DOSAGE
Ephedrine are administered intramuscularly, subcutaneously or intravenously. The route of administration should be determined by the needs of individual patients; patients who need an immediate response or who are in shock may require intravenous administration to ensure absorption of the drug.

If ephedrine is administered parenterally to relieve severe, acute bronchospasm, the smallest effective dose (usually 12.5 to 25 mg) should be given. Further dosage should be determined by patient response.

When used as a pressor agent, ephedrine should be administered in the lowest effective dosage for the shortest possible time. The usual adult subcutaneous or intramuscular dose is 25 to 50mg (range: 10 to 50 mg); further dosage should be determined by blood pressure response. For direct intravenous injection, 5 to 25 mg of the drug may be administered slowly; if necessary to achieve the desired response, additional intravenous doses may be given in 5 to 10 minutes. The parenteral adult dose should not exceed 150 mg in 24 hours. Children may receive 0.5mg/kg or 16.7 mg/m^2 subcutaneously or intramuscularly every 4 to 6 hours; alternatively, a dosage of 0.75 mg/kg or 25 mg/m^2 may be administered subcutaneously or by intravenous injection 4 times daily or as otherwise determined by the patient's response.

Pharmaniaga Ephedrine Hydrochloride 30mg/ml Injection is compatible with sodium chloride 9mg/ml (0.9%), Ringer's Lactate solution and glucose 50mg/ml (5%).

ROUTE OF ADMINISTRATION
Parenteral
(Intramuscular, Subcutaneous or Slow Intravenous Injection)

CONTRAINDICATIONS
Ephedrine is contraindicated in patients with coronary thrombosis, thyrotoxicosis, hypertension and close angle glaucoma. Ephedrine is also contraindicated in patients with known hypersensitivity to ephedrine or other sympathomimetic agents. (e.g. phenylpropanolamine, phenylephrine, pseudoephedrine and methylphenidate. Ephedrine is also contraindicated in combination with alpha sympathomimetic agents and combination with non-selective Monoamine Oxidase Inhibitors (MAOI) or within 14 days of their withdrawal.

WARNINGS AND PRECAUTIONS
Warnings
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 selective MAO inhibitors.

Ephedrine increases blood pressure and therefore special care is advisable in patients receiving antihypertensive therapy. Interactions of Ephedrine with alphaand betablocking drugs may be complex. Propranolol and other betaadrenoceptor blocking agents antagonise the effects of beta2 adrenoceptor stimulants (beta2 agonists) such as salbutamol.

Adverse metabolic effects of high doses of beta2 agonists may be exacerbated by concomitant administration of high doses of corticosteroids; patients should therefore be monitored carefully when the 2 forms of therapy are used together although this precaution is not so applicable to inhaled corticotherapy. Hypokalaemia associated with high doses of beta2 agonists may result in increased susceptibility to digitalisinduced cardiac arrhythmias. Hypokalaemia may be enhanced by concomitant administration of aminophylline or other xanthines, corticosteroids, or by diuretic therapy.

Precautions
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 antidoping tests.

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

INTERACTION WITH OTHER MEDICAMENTS
Ephedrine interacts with glucocorticoid, adrenocorticoids, corticotropine, urinary alkalisers, alpha-adrenergic blocking agents, diatrizoates, iothalamate, ioxaglate, ergot alkaloids, methysergide, oxytoxin, doxapram, guanadrel, guanethidine, mazindol, mecamylamine, methyldopa, trimethaphan, methylphenidate and rauwolfia alkaloids.

Incompatibilities
Ephedrine injection have been reported to be incompatible with various drugs, but the compatibility depends on several factors (e.g concentration of the drugs, resulting pH, and temperature).

STATEMENT ON USAGE DURING PREGNANCY AND LACTATION
Pregnancy
Parenteral administration of ephedrine to maintain blood pressure during spinal anaesthesia for delivery can cause acceleration of foetal heart rate, and should not be used when maternal blood pressure exceeds 130/80.

Lactation
Ephedrine is excreted in breast milk, use by nursing mother is not recommended because of higher than usual risk for infant.

SIDE EFFECTS
Ephedrine most common adverse effects are tachycardia, anxiety, restlessness and insomnia. Tremor, dry mouth, impaired calculation to the extremities, hypertension, and cardiac arrhythmias may also occur.

Ephedrine may be used in labour to maintain blood pressure during spinal anaesthesia but can cause fetal tachycardia. Paranoid psychosis, delusions and hallucinations may also follow ephedrine overdosage.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

Symptoms

Giddiness, headache, nausea, vomiting, fever, sweating, thirst, tachycardia, precordial pain, palpitations, difficulty in micturition, muscular weakness and tremors, anxiety, restlessness and insomnia.

Hypertension and ventricular arrhythmias may occur more rarely. Paranoid psychosis, delusion and hallucinations convulsions, respiratory depression and coma may also occur.

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

Treatment

- Slow intravenous injection of Labetalol 50-200mg may be given with electrocardiograph monitoring for the treatment of supraventricular tachycardia. Marked hypokalaemia (<2.8 mmol/l) 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.
- For supraventricular or ventricular tachycardias, administering a beta adrenergic blocker, such as propranolol, by slow intravenous administration if necessary to control cardiac arrhythmias; however, in asthmatic patients, a cardioselective beta-adrenergic blocker (e.g. acebutolol, atenolol, metoprolol) may be more appropriate. The betablocker should be used with caution in asthmatic patients because it could induce severe bronchospasm or an asthmatic attack.
- 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.

Other treatment also includes:

- Protecting patient's airway and supporting ventilation and perfusion.
- Monitoring and maintaining, within acceptable limits, patient's vital signs, blood gases and serum electrolytes. Also, monitoring electrocardiogram continuously.
- For marked hypertension, administering nitroprusside or phento-amine infusion, if necessary.
- For "true" hypotension, administration of intravenous fluids, elevation of legs, or administration of inotropic vasopressors, such as norephinephrine, should be considered.
- To control convulsions, administer diazepam. For refractory seizures, general anaesthesia with thiopental or halothane and paralysis with a neuromuscular blocking agent may be necessary.
- Controlling pyrexia by cool applications and by slow intravenous administration of 1 mg of dexamethasone per kg body weight.

INSTRUCTION FOR USE

For single use only.

Ephedrine hydrochloride is compatible with sodium chloride 9 mg/ml (0.9%), Ringer's lactate solution and glucose 50 mg/ml (5%).

The drug product should be examined visually and should not be used if particulate matter or discolouration are present.

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

STORAGE CONDITION

Store below 30°C. Protect from light. Retain in carton until time of use.

Pharmaniaga Ephedrine Hydrochloride 30mg/ml Injection is compatible with the following infusion solutions:

- Sodium Chloride 9mg/ml (0.9%)
- Ringer's Lactate Solution
- Glucose 50mg/ml (5%)

After dilution, the solution must be used within 72 hours at temperature below 30°C and up to 24 hours at temperature 2-8°C after diluted with the compatible solutions listed above.

SHELF LIFE

2 years.

Pharmaniaga Ephedrine Hydrochloride 30mg/ml Injection is compatible with the following infusion solutions:

- Sodium Chloride 9mg/ml (0.9%)
- Ringer's Lactate Solution
- Glucose 50mg/ml (5%)

After dilution, the solution must be used within 72 hours at temperature below 30°C and up to 24 hours at temperature 2-8°C after diluted with the compatible solutions listed above.

DOSAGE FORMS AND PACKAGING AVAILABLE:

10 x 1mL ampoule (clear).

PRODUCT REGISTRATION HOLDER/MANUFACTURER:
PHARMANIAGA LIFESCIENCE SDN BHD (198201002939)

Lot 7, Jalan PPU 3,
Taman Perindustrian Puchong Utama,
47100 Puchong,Selangor Darul Ehsan,
MALAYSIA

2002086

Revision Date: 10-Jun-2020