SCHEDULING STATUS: S6

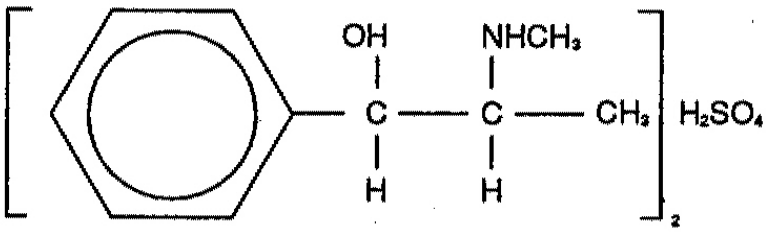
PROPRIETARY NAME (and dosage form):

EPHEDRINE SULPHATE INJECTION 50 mg/ml Solution for injection, ampoule

COMPOSITION:

EPHEDRINE SULPHATE INJECTION 50 mg/ml is a sterile, non-pyrogenic solution containing ephedrine sulphate 50 mg/ml in water for injection. It is administered by subcutaneous, intramuscular or intravenous injection as an adrenergic agent. The solution contains no bacteriostat, antimicrobial agent or added buffer. The pH is 5,3 (approximately). The osmolar concentration of the 5 % solution is 0,35 mOsm/l (calc.).

Ephedrine sulphate is a sympathomimetic amine, chemically designated alpha [1-(methylamino) ethyl] benzenemethanol sulphate (2:1) (salt). It has the following structural formula:



PHARMACOLOGICAL CLASSIFICATION:

A 5.1 Adrenomimetics (sympathomimetics)

PHARMACOLOGICAL ACTION:

Therapeutic doses of ephedrine produce mainly relaxation of smooth muscle and, if norepinephrine stores are intact, cardiac stimulation and increased systolic and usually increased diastolic blood pressure. Its vasopressor effect results largely from increased cardiac output and to a lesser extent from peripheral vasoconstriction.

Ephedrine stimulates both alpha and beta receptors and its peripheral actions are due partly to norepinephrine release and partly to a direct effect on receptors.

Ephedrine may deplete norepinephrine stores in sympathetic nerve endings, so that tachyphylaxis to cardiac and pressor effects of the drug may develop. Central nervous system effects are similar to those of amphetamine drugs but less pronounced. The central effects of ephedrine are overshadowed to a large extent by its peripheral actions.

Glycogenolysis in the liver is increased by ephedrine; usual doses of ephedrine are unlikely to produce hyperglycaemia. Ephedrine increases oxygen consumption and metabolic rate as a probable result of central stimulation.

Ephedrine is rapidly and completely absorbed following parenteral injection. Pressor and cardiac responses to ephedrine persist for one hour following intramuscular or subcutaneous administration of 25 to 50 mg.

Small amounts of ephedrine are slowly metabolised in the liver; metabolites have been identified as p-hydroxyephedrine, p-hydroxynorephedrine, norephedrine, and conjugates of these compounds. The drug and its metabolites are excreted in the urine, mostly as unchanged ephedrine. Rate of urinary excretion is dependent on urinary pH. Percentage excretion of the drug and its metabolites is increased by acidification of the urine. Elimination half-life of the drug has been reported to be about three hours when the urine is acidified to pH 5 and about six hours when urinary pH is 6,3.

INDICATIONS:

EPHEDRINE SULPHATE INJECTION 50 mg/ml is indicated to counteract the hypotensive effects of spinal or other types of non-topical conduction anaesthesia. It is useful as a pressor agent in hypotensive states.

CONTRAINDICATIONS:

Ephedrine is contraindicated in patients with known hypersensitivity to sympathomimetic amines and in patients with angle closure glaucoma. It should not be used in patients anaesthetised with halogenated hydrocarbons as these agents may sensitise the heart to the arrhythmic action of sympathomimetic drugs.

WARNINGS:

Ephedrine may cause hypertension resulting in intracranial haemorrhage. Ephedrine may induce anginal pain in patients with coronary insufficiency or ischaemic heart disease. The drug may also induce potentially fatal arrhythmias in patients with organic heart disease or who are receiving drugs that sensitise the myocardium.

Initially, parenterally-administered ephedrine may produce constriction of renal blood vessels and decreased urine formation.

DOSAGE AND DIRECTIONS FOR USE:

Depending on the clinical circumstances, **EPHEDRINE SULPHATE INJECTION 50 mg/ml** may be given subcutaneously, intramuscularly or intravenously.

Usual adult dose: 25 to 50 mg (range 10 to 50 mg) injected subcutaneously or intramuscularly (equivalent to 0,2 to 1,0 ml of 5 % solution) is usually adequate to prevent or minimise hypotension secondary to spinal anaesthesia. Repeat doses should be governed by blood pressure response. Absorption (onset of action) by the intramuscular route is more rapid (within 10 to 20 minutes) than by subcutaneous injection. The intravenous route may be used if an immediate effect is desired, at a dosage of 5 – 10 mg.

When used during labour, administer only sufficient dosage to maintain blood pressure at or below 130/80 mmHg.

Usual paediatric dose: 750 micrograms per kg of body weight or 25 mg/m^2 of body surface injected intravenously or subcutaneously.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit (see **Special precautions**).

SIDE EFFECTS AND SPECIAL PRECAUTIONS:

Acute toxic effects are usually extensions of the therapeutic actions of the drug. A sharp rise in blood pressure sufficient to produce cerebral haemorrhage may occur. Other effects include headache, restlessness, anxiety, tension, tremor, weakness, dizziness, confusion, delirium hallucinations, pallor, respiratory difficulty, palpitation, sweating, nausea or vomiting. Repeated injections may cause

contraction of the bladder sphincter and interfere with voluntary urination. The possibility of urinary retention, especially in the elderly male, should be kept in mind.

Initially, parenterally administered ephedrine may produce constriction of renal blood vessels and decrease urine formation.

Special precautions:

EPHEDRINE SULPHATE INJECTION 50 mg/ml is subject to oxidation and should be protected against exposure to light.

Do not administer unless solution is clear and seal is intact. Discard unused portion.

Ephedrine should be used cautiously in patients with hyperthyroidism, hypertension, heart disease (including coronary insufficiency, angina pectoris and patients receiving digitalis), cardiac arrhythmias, diabetes, unstable vasomotor system, or in patients taking monoamine oxidase (MAO) inhibitors.

DRUG INTERACTIONS:

Ephedrine should not be administered concomitantly with other sympathomimetic drugs because of possible additive effects and increased toxicity.

Alpha-adrenergic blocking agents may reduce the vasopressor response to ephedrine by causing vasodilation.

Beta-adrenergic blocking drugs may block the cardiac and bronchodilating effects of ephedrine.

Administration of ephedrine to patients receiving anaesthesia with halogenated hydrocarbons such as halothane which sensitise the myocardium, may induce cardiac arrhythmia (see **CONTRAINDICATIONS**).

If a pressor drug is required in patients receiving myocardial sensitising anaesthetics, one with less cardiac stimulating effects should be considered. When encountered, such arrhythmias may respond to administration of a beta-adrenergic blocking drug.

Ephedrine also should be used cautiously with other drugs (e.g. digitalis glycosides) that sensitise the myocardium to the actions of sympathomimetic agents.

Drugs such as reserpine and methyldopa, which reduce the amount of norepinephrine in sympathetic nerve endings, may reduce the pressor response to ephedrine. Diuretic agents also may decrease the vascular response to ephedrine.

Ephedrine may antagonise the neuron blockade produced by guanethidine, resulting in decreased antihypertensive effect and requiring increased dosage of the latter.

PREGNANCY:

Safety in pregnancy has not been established.

LABOUR AND DELIVERY:

Parenteral administration of ephedrine to maintain blood pressure during low or other spinal anaesthesia for delivery can cause acceleration of foetal heart rate and should not be used in obstetrics when maternal blood pressure exceeds 130/80 mmHg.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Continued injections of ephedrine (after depletion of norepinephrine from the nerve endings with loss of vasopressor effect) may result in hypotension more serious than that existing prior to the use of ephedrine. In the absence of norepinephrine depletion, excessive parenteral dosage produces tachycardia, exaggerated rise in blood pressure plus central nervous system effects.
In the event of adverse blood pressure effects, the drug should be stopped and appropriate corrective measures instituted.

CONDITIONS OF REGISTRATION:

Advertising to the professions only.

IDENTIFICATION:

Clear, colourless solution which is sterile and non-pyrogenic.

PRESENTATION:

EPHEDRINE SULPHATE INJECTION 50 mg/ml is supplied in 1 ml single-dose ampoules. Ten ampoules are packed into a tray, which is in turn packed into a carton.

STORAGE INSTRUCTIONS:

Store in a cool (at or below 25 °C) place.

Protect from light until ready to use.

Keep out of reach of children.

REGISTRATION NUMBER:

RX/5.1/252

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

Pfizer Laboratories (Pty) Ltd

85 Bute Lane

Sandton, 2196

South Africa

DATE OF PUBLICATION OF THIS PACKAGE INSERT:

31 January 1985

Manufacturer: Hospira SpA, Liscate, Italy

BOTSWANA: S4

Reg.No.: B9322170

NAMIBIA: S4

Reg. No.: 90/5.1/0055