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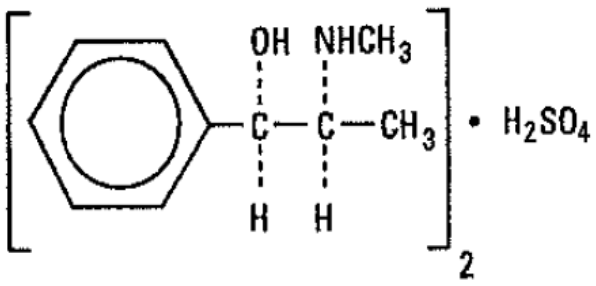
EPHEDRINE SULFATE Injection, USP (50 mg/mL)

Preservative-Free
Ampul
Protect from light.
Keep ampuls in tray until time of use.

DESCRIPTION

Ephedrine Sulfate Injection, USP is a sterile, nonpyrogenic solution containing ephedrine sulfate 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 (4.5 to 7.0). The osmolar concentration of the 5% solution is 0.35 mOsmol/mL (calc.).

Ephedrine Sulfate, USP is a sympathomimetic amine chemically designatedα-[1-(methylamino) ethyl] benzenemethanol sulfate (2:1) (salt). It has the following structural formula:



CLINICAL PHARMACOLOGY

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. Pressor responses to parenteral ephedrine are slower but more prolonged than those produced by epinephrine. Ephedrine stimulates both alpha and beta receptors and its peripheral actions are due partly to norepinephrine release and party to 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 but not as much as by epinephrine; usual doses of ephedrine are unlikely to produce hyperglycemia. 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 metabolized 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 AND USAGE

Ephedrine Sulfate Injection, USP is indicated primarily to counteract the hypotensive effect of spinal or other types of nontopical conduction anesthesia. It is also useful as a pressor agent in hypotensive states following sympathectomy, or following overdosage with ganglionic blocking agents, antiadrenergic agents, veratrum alkaloids or other drugs used for lowering blood pressure in the treatment of arterial hypertension. The drug is sometimes injected to relieve acute bronchospasm, but it is less effective than epinephrine for this purpose.

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 anesthetized with agents such as cyclopropane or halothane as these agents may sensitize the heart to the arrhythmic action of sympathomimetic drugs.

Ephedrine should not ordinarily be used in those cases where vasopressor drugs may be contraindicated, e.g., in thyrotoxicosis, diabetes, in obstetrics when maternal blood pressure is in excess of 130/80 and in hypertension and other cardiovascular disorders.

WARNINGS

Ephedrine may cause hypertension resulting in intracranial hemorrhage. Ephedrine may induce anginal pain in patients with coronary insufficiency or ischemic heart disease. The drug also may induce potentially fatal arrhythmias in patients with organic heart disease or who are receiving drugs that sensitize the myocardium. See CONTRAINDICATIONS.
Initially, parenterally administered ephedrine may produce constriction of renal blood vessels and decreased urine formation.

PRECAUTIONS

Ephedrine Sulfate Injection, USP is subject to oxidation and should be protected against exposure to light.

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

Except as a temporary expedient to maintain cerebral and coronary circulation pending restoration of adequate circulating blood volume, Ephedrine Sulfate Injection USP should not be used to overcome hypotension due to acute hemorrhagic or non-cardiogenic shock.

Pregnancy
Animal reproduction studies have not been conducted with ephedrine. It is also not known whether ephedrine can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Therefore, ephedrine should be given to a pregnant woman only if the benefits outweigh possible risks.

Labor and Delivery
Parenteral administration of ephedrine to maintain blood pressure during low or other spinal anesthesia for delivery can cause acceleration of fetal heart rate and should not be used in obstetrics when maternal blood pressure exceeds 130/80. See CONTRAINDICATIONS.

Drug Interactions
All vasopressors should be used cautiously in patients taking monoamine oxidase (MAO) inhibitors.

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 anesthesia with cyclopropane or halogenated hydrocarbons such as halothane which sensitize the myocardium, may induce cardiac arrhythmia. (See CONTRAINDICATIONS). Use of a pressor drug with less cardiac stimulating effects should be considered in patients receiving myocardial sensitizing anesthetics. 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 sensitize 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 vascular response to pressor drugs such as ephedrine.

Ephedrine may antagonize the neuron blockade produced by guanethidine resulting in decreased anti-hypertensive effect and requiring increased dosage of the latter.

Pediatric Use
The safety and effectiveness of Ephedrine has not been established, its limited use in pediatric patients has been inadequate to fully define the proper dosage and limitations of use.

ADVERSE REACTIONS

Acute toxic effects are usually extensions of the therapeutic actions of the drug and are most often due to overdosage. Excessive doses may cause a sharp rise in blood pressure sufficient to produce cerebral hemorrhage. Other effects (usually transient) 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.

DRUG ABUSE AND DEPENDENCE

None known with parenteral form.

OVERDOSAGE

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, and possible cerebrovascular bleeding, plus central nervous system effects. In the event of adverse blood pressure effects, the drug should be stopped and appropriate corrective measures instituted. See ADVERSE REACTIONS.

DOSAGE AND ADMINISTRATION

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

Do not administer unless solution is clear and seal is intact.

Depending on the clinical circumstances, Ephedrine Sulfate Injection USP 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 minimize hypotension secondary to spinal anesthesia. Repeat doses should be governed by blood pressure response or, if used as a bronchodilator, according to the degree of improvement 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.

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

In acute attacks of asthma, the smallest effective dose should be used (usually 0.25 to 0.5 mL) or as otherwise determined by the patient's response.

Usual Pediatric Dose
750 micrograms per kg of body weight or 25 mg/m^2 of body surface injected intravenously or subcutaneously, 4 times daily or as otherwise determined by the patient's response.

STABILITY AND STORAGE RECOMMENDATIONS

Store at 20 to 25°C [68 to 77°F). [See USP Controlled Room Temperature.]
Discard unused portion.

HOW SUPPLIED

Ephedrine Sulfate Injection, USP (50 mg/mL) is supplied in a 1 mL single-dose ampul (List No. 3073).

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