

Important Prescribing Information

Subject: New Formulation of Adrenalin® (epinephrine) Injection 1-mL Single-use Vials: Withdrawal of Intraocular Surgery Indication

Dear Healthcare Provider,

Par Pharmaceutical would like to bring to your attention to a new formulation of Adrenalin® (epinephrine) Injection 1-mL single-use vials. Due to the addition of the inactive ingredient, tartaric acid, this new formulation is not approved for intraocular use and the indication of induction and maintenance of mydriasis during intraocular surgery has been removed from the Prescribing Information.

Important Prescribing Information

The updated formulation of Adrenalin® (epinephrine) Injection contains tartaric acid to improve product stability. The safety of tartaric acid in the levels present in Adrenalin® (epinephrine) Injection has not been established for intraocular use or intracameral injection.

When the original formulation of Adrenalin® (epinephrine) Injection 1 mg/mL is used during intraocular surgery, it must first be diluted with 100 to 1000 mL of an ophthalmic irrigation fluid to create an epinephrine concentration of 10 µg/mL to 1 µg/mL. Since the updated formulation of Adrenalin® (epinephrine) Injection contains 2.25 mg tartaric acid per mL, should it be inadvertently used, the resulting ophthalmic irrigation solution will contain 22.5 µg to 2.25 µg of tartaric acid per mL. There is no experience with intracameral injection administration of solutions containing tartaric acid.

Reporting Adverse Events

Healthcare providers and patients are encouraged to report adverse events in patients inadvertently exposed to the new formulation of Adrenalin® (epinephrine) Injection during intraocular surgery to Par Pharmaceutical at 1-800-828-9393 or drugsafety@parpharm.com. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

You may also contact our medical information department at 1-800-828-9393 or drugsafety@parpharm.com if you have any questions about the information contained in this letter or the safe and effective use of the new formulation of Adrenalin® (epinephrine) Injection.

This letter is not intended as a complete description of the benefits and risks related to the intraocular use of the new formulation of Adrenalin® (epinephrine) Injection. Please refer to the summary prescribing information on back.

Sincerely,

Toni Picone
Director of Marketing, Par Sterile Products

INDICATION

Adrenalin is a non-selective alpha and beta adrenergic agonist indicated for emergency treatment of allergic reactions (Type 1), including anaphylaxis.

IMPORTANT SAFETY INFORMATION FOR ADRENALIN

- Adrenalin (epinephrine injection) should not be injected into buttocks, digits, hands, or feet.
- Administer Adrenalin with caution when used intramuscularly or subcutaneously as this may aggravate angina pectoris or produce ventricular arrhythmias, particularly in patients with underlying heart disease.
- Patients with hyperthyroidism, Parkinson's disease, diabetes, and pheochromocytoma are at greater risk of having adverse reactions when used intramuscularly or subcutaneously.
- Common adverse reactions to systemically administered epinephrine include anxiety, apprehensiveness, restlessness, tremor, weakness, dizziness, sweating, palpitations, pallor, nausea and vomiting, headache, and respiratory difficulties.
- Arrhythmias, including fatal ventricular fibrillation, rapid rises in blood pressure producing cerebral hemorrhage, and angina have occurred with use of Adrenalin.
- Elderly patients and pregnant women may be at greater risk of developing adverse reactions when Adrenalin is administered parenterally.
- Possible drug interactions with the following: sympathomimetic agents, cardiac glycosides, halogenated hydrocarbon anesthetics, diuretics, tricyclic antidepressants, MAO inhibitors, levothyroxine sodium, certain antihistamines, ergot alkaloids, alpha- and beta-adrenergic blocking drugs

Please see summary of prescribing information on back.

For Full Prescribing Information, please refer to the following link on our website:
<http://www.parsterileproducts.com/products/products/adrenalin-injection.php>

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Adrenalin® (epinephrine injection) 1 mg/mL (1:1000) for intramuscular and subcutaneous use

**Brief summary of prescribing information
(For complete prescribing information please see package insert)**

INDICATIONS AND USAGE

Adrenalin is a non-selective alpha and beta adrenergic agonist indicated for emergency treatment of allergic reactions (Type 1), including anaphylaxis.

DOSAGE AND ADMINISTRATION

Dosing Guidelines for Anaphylaxis

- *Adults and Children 30 kg (66 lbs) or more:* 0.3 to 0.5 mg (0.3 to 0.5 mL) intramuscularly or subcutaneously into anterolateral aspect of the thigh every 5 to 10 minutes as necessary
- *Children 30 kg (66 lbs) or less:* 0.01 mg/kg (0.01 mL/kg), up to 0.3 mg (0.3 mL), intramuscularly or subcutaneously into anterolateral aspect of the thigh every 5 to 10 minutes as necessary

DOSAGE FORMS AND STRENGTHS

Injection: 1 mg/mL (1:1000), 1 mL single-use vials and 30 mL multiple-dose vials

CONTRAINDICATIONS

None.

WARNINGS AND PRECAUTIONS

- Do not inject into buttocks, digits, hands, or feet.
- Rare cases of serious skin and soft tissue infections have been reported following epinephrine injection. Advise patients to seek medical care if they develop signs or symptoms of infection.
- May aggravate angina pectoris or produce ventricular arrhythmias, particularly in patients with underlying heart disease, administer with caution when used intramuscularly or subcutaneously.
- Patients with hyperthyroidism, Parkinson's disease, diabetes, and pheochromocytoma are at greater risk of having adverse reactions when used intramuscularly or subcutaneously.
- Presence of sulfite in this product should not deter use for anaphylaxis.

ADVERSE REACTIONS

Common adverse reactions to systemically administered epinephrine include anxiety, apprehensiveness, restlessness, tremor, weakness, dizziness, sweating, palpitations, pallor, nausea and vomiting, headache, and respiratory difficulties. Arrhythmias, including fatal ventricular fibrillation, rapid rises in blood pressure producing cerebral hemorrhage, and angina have occurred.

DRUG INTERACTIONS

Sympathomimetic Agents, Tricyclic Antidepressants

Co-administration of Adrenalin with sympathomimetic agents, tricyclic antidepressants is likely to lead to an enhancement of effects.

Cardiac Glycosides, Digitalis, Diuretics, Quinidine, Antiarrhythmic Agents, Halogenated Hydrocarbon General Anesthetics

Concomitant use of Adrenalin with cardiac glycosides, digitalis, diuretics, quinidine, antiarrhythmic agents, halogenated hydrocarbon general anesthetics may result in cardiac arrhythmias.

Ergot Alkaloids, Phenothiazines, Alpha- and Beta-blockers

Do not use Epinephrine with these agents.

USE IN SPECIFIC POPULATIONS

Pregnancy

Pregnancy Category C:

There are no adequate and well-controlled studies of Adrenalin in pregnant women. Epinephrine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Epinephrine is teratogenic in rabbits, mice and hamsters.

Labor and Delivery

Epinephrine should be used with caution during labor and delivery as it may result in uterine vasoconstriction, decreased uterine blood flow, fetal anoxia.

Nursing Mothers

It is not known whether epinephrine is excreted in human milk. Caution should be exercised when epinephrine is administered to a nursing woman because many drugs are excreted in human milk.

Pediatric Use

Clinical use data support weight-based dosing for treatment of anaphylaxis in pediatric patients, and other reported clinical experience with the use of epinephrine suggests that the adverse reactions seen in children are similar in nature and extent to those both expected and reported in adults.

Geriatric Use

Clinical studies for the treatment of anaphylaxis have not been performed in subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience with use of epinephrine for the treatment of anaphylaxis has identified that geriatric patients may be particularly sensitive to the effects of epinephrine. Thus, consider starting with a lower dose of epinephrine in geriatric patients to take into account potential concomitant disease or other drug therapy.

OVERDOSAGE

Overdosage of epinephrine may result in extremely elevated arterial pressure, cerebrovascular hemorrhage (particularly in elderly patients), pulmonary edema, myocardial ischemia, myocardial infarction, and cardiomyopathy, extreme pallor and coldness of the skin, metabolic acidosis due to elevated blood lactic acid levels, kidney failure, transient bradycardia followed by tachycardia and these may be accompanied by potentially fatal cardiac arrhythmias. Suitable corrective measures must be taken in such situations. Epinephrine is rapidly inactivated in the body and treatment following overdose with epinephrine is primarily supportive.

DESCRIPTION

Adrenalin® (epinephrine injection, USP) is a clear, colorless, sterile solution containing 1 mg/mL (1:1000) epinephrine, packaged as 1 mL of solution in a single-use clear glass vial or 30 mL of solution in a multiple-dose amber glass vial. In the 1 mL vial, each 1 mL of Adrenalin® solution contains 1 mg epinephrine, 7.3 mg sodium chloride, 0.457 mg sodium metabisulfite, 1 mg sodium hydroxide, 2.25 mg tartaric acid, 0.20 mg disodium edetate dihydrate, hydrochloric acid to adjust pH, and water for injection. In the 30 mL vial, each 1 mL of Adrenalin® solution contains 1 mg epinephrine, 6.15 mg sodium chloride, 0.457 mg sodium metabisulfite, 0.920 mg sodium hydroxide, 2.25 mg tartaric acid, 0.20 mg disodium edetate dihydrate, hydrochloric acid to adjust pH, 5.25 mg chlorobutanol as a preservative and water for injection. The pH range is 2.2-5.0.

HOW SUPPLIED/STORAGE AND HANDLING

Adrenalin® 1 mL Single-Use Vials:

NDC 42023-159-25: Each carton contains 25 single-use vials containing 1 mL Adrenalin® (epinephrine injection, USP) solution 1 mg/mL (1:1000) in a 3 mL clear glass vial.

Adrenalin® 30 mL Multi-Dose Vials:

NDC 42023-168-01: Each carton contains 1 multiple-dose vial containing 30 mL Adrenalin® (epinephrine injection, USP) solution 1 mg/mL (1:1000) in a 36 mL amber glass vial.

Vial and contents must be discarded 30 days after initial use.

Store between 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature]. Epinephrine is light sensitive. Protect from light and freezing.

Inspect visually for particulate matter and discoloration prior to administration. Do not use the solution if it is colored or cloudy, or if it contains particulate matter.

Distributed by:

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