



Simple to use when it counts.



Prescribing Summary



Patient Selection Criteria

THERAPEUTIC CLASSIFICATION

Sterile epinephrine injection USP

INDICATIONS AND CLINICAL USE

EpiPen® and EpiPen® Jr (0.3 and 0.15 mg epinephrine) Auto-injectors ("EpiPen") are indicated for the emergency treatment of anaphylactic reactions in patients who are determined to be at increased risk for anaphylaxis, including individuals with a history of anaphylactic reactions. Selection of the appropriate dosage strength is determined according to patient body weight. EpiPen and EpiPen Jr are intended for immediate self-administration for the emergency treatment of severe allergic reactions (Type I), including anaphylaxis associated with:

- foods (e.g., peanuts, tree nuts, shellfish, fish, milk, eggs, and wheat)
- stinging insects (e.g., Order Hymenoptera, including bees, wasps, hornets, yellow jackets, and fire ants) and biting insects (e.g., mosquitoes and black flies)
- medications
- latex
- other allergens
- idiopathic anaphylaxis
- exercise-induced anaphylaxis.

Epinephrine is the drug of choice for the emergency treatment of severe allergic reactions. The strong vasoconstrictor action of epinephrine, through its effect on alpha adrenergic receptors, quickly counteracts vasodilation and increased vascular permeability which can lead to loss of intravascular fluid volume and hypotension during anaphylactic reactions. EpiPen and EpiPen Jr are designed as emergency supportive therapy only and not as a replacement or substitute for subsequent medical or hospital care, nor are they intended to supplant insect venom hyposensitization. Anaphylaxis is a serious, acute, allergic reaction that may cause death. It has a sudden onset and generally lasts less than 24 hours. Because anaphylaxis is a generalized reaction, a wide variety of clinical signs and symptoms may be observed. One to 2% of the general population are estimated to be at risk for anaphylaxis from food allergies and insect stings, with a lower reported prevalence for drugs and latex. People with asthma are at particular risk.

Clinical Signs and Symptoms of Anaphylaxis Oral: pruritus of lips, tongue, and palate, edema of lips and tongue; metallic taste in the mouth. **Cutaneous:** flushing, pruritus, urticaria, angioedema, morbilliform rash, and pilor erecti. **Gastrointestinal:** nausea, abdominal pain, vomiting, and diarrhea. **Respiratory:** Laryngeal: pruritus and "tightness" in the throat, dysphagia, dysphonia, hoarseness, wheezing, and cough; Nasal: nasal pruritus, congestion, rhinorrhea, sneezing, and sensation of itching in the external auditory canals. **Cardiovascular:** feeling of faintness, syncope, chest pain, dysrhythmia, hypotension. **Note:** Hypotension is a sign of anaphylaxis. Patients should be treated in the early stages of anaphylaxis to prevent hypotension from developing. **Other:** periorbital pruritus, erythema and edema, conjunctival erythema, and tearing; lower back pain and uterine contractions in women; aura of "doom." The severity of previous anaphylactic reactions does not determine the severity of future reactions, and subsequent reactions could be the same, better, or worse. The severity may depend on the degree of sensitivity, the dose of allergen, and other factors. Research shows that fatalities from anaphylaxis are often associated with failure to use epinephrine or a delay in the use of epinephrine treatment. Epinephrine should be administered as early as possible after the onset of symptoms of a severe allergic response. Patients requiring epinephrine will not always have predictable reactions. Adequate warning signs are not always present before serious reactions occur. It is recommended that epinephrine be given at the start of any reaction associated with a known or suspected allergen contact. In patients with a history of severe cardiovascular collapse on exposure to an allergen, the physician may advise that epinephrine be administered immediately after exposure to that allergen, and before any reaction has begun. Epinephrine may prove to be life saving when used as directed immediately following exposure to an allergen. In most patients, epinephrine is effective after 1 injection. However, symptoms may recur and further injections may be required to control the reaction. Epinephrine can be re-injected every 5 to 15 minutes until there is resolution of the anaphylaxis or signs of adrenaline excess (such as palpitations, tremor, uncomfortable apprehension and anxiety). All individuals receiving emergency epinephrine must be immediately transported to hospital, ideally by ambulance, for evaluation and observation. Repeat attacks have occurred hours later without additional exposure to the offending allergen. Therefore, it is recommended that a patient suffering from an anaphylactic reaction be observed in an emergency facility for an appropriate period because of the possibility of either a "biphasic" reaction (a second reaction) or a prolonged reaction. At least a four hour period of observation is advised, although this time may vary. The attending physician will take into consideration such factors as the severity of the reaction, the patient's response and history and the distance from the hospital to the patient's home. Anaphylactic reactions typically follow a uniphasic course; however, 20% will be biphasic in nature. The second phase usually occurs after an asymptomatic period of 1 to 8 hours, but may occur up to 38 hours (mean 10 hours) after the initial reaction. About one third of the second-phase reactions are more severe, one third are as severe, and one third are less severe. The second-phase reactions can occur even following administration of corticosteroids. **Following treatment of anaphylaxis, the patient must stay within close proximity to a**

hospital or where he or she can call 911 for the next 48 hours. Protracted anaphylaxis, which is frequently associated with profound hypotension and sometimes lasts longer than 24 hours, is minimally responsive to aggressive therapy, and has a poor prognosis.

CONTRAINDICATIONS

There are no absolute contraindications to the use of epinephrine in a life-threatening allergic situation.



Safety Information

WARNINGS AND PRECAUTIONS

Patients with a history of anaphylaxis are at risk for subsequent episodes and even death. All patients who have had one or more episodes of anaphylaxis should have injectable epinephrine with them or with their parent or caregiver at all times, and should wear some form of medical identification bracelet or necklace. Following the resolution of an anaphylactic episode and discharge from hospital, the patient should immediately obtain and fill a new EpiPen or EpiPen Jr prescription. Epinephrine injection (1:1000 and 1:2000) is not intended as a substitute for medical attention or hospital care. In conjunction with the administration of epinephrine, the patient should seek appropriate medical care. Antihistamines and asthma medications must not be used as first line treatment for an anaphylactic reaction. Accidental injection into the hands or feet may result in loss of blood flow to the affected areas and should be avoided. If there is an accidental injection into these areas, the patient must go immediately to the nearest emergency room for treatment. Epinephrine should only be injected into the anterolateral aspect of the thigh. Every effort should be made to avoid possible inadvertent intravascular administration through appropriate selection of an injection site such as the thigh. Do not inject into the buttock. Large doses or accidental intravenous injection of epinephrine may result in cerebral hemorrhage due to a sharp rise in blood pressure. Rapidly acting vasodilators can counteract the marked pressor effects of epinephrine. The presence of a condition listed below is not a contraindication to epinephrine administration in an acute, life-threatening situation. Therefore, patients with these conditions, or any other person who might be in a position to administer epinephrine to a patient with these conditions experiencing anaphylaxis, should be instructed about the circumstances under which epinephrine should be used: **Cardiovascular** Epinephrine use should be avoided in patients with cardiogenic, traumatic, or hemorrhagic shock; cardiac dilation; and/or cerebral arteriosclerosis. Epinephrine should be used with caution in patients with cardiac arrhythmias, coronary artery or organic heart disease, hypertension, or in patients who are on medications that may sensitize the heart to arrhythmias, e.g., digitalis, diuretics, or anti-arrhythmics. In such patients, epinephrine may precipitate or aggravate angina pectoris as well as produce ventricular arrhythmias. Patients with hypertension or hyperthyroidism are prone to more severe or persistent effects. **Endocrine and Metabolism** Patients with diabetes may develop increased blood glucose levels following epinephrine administration. **Neurologic** Epinephrine use should be avoided in patients with organic brain damage. Patients with Parkinson's disease may notice a temporary worsening of symptoms after treatment with epinephrine. **Ophthalmologic** Epinephrine use should be avoided in patients with narrow-angle glaucoma. **Respiratory** There is a significantly increased risk of respiratory symptoms in patients with concomitant asthma, especially if poorly controlled. These patients are at increased risk of death from anaphylaxis. Fatalities may also occur from pulmonary edema resulting from peripheral constriction and cardiac stimulation. **Sensitivity** This product contains sodium metabisulfite, a substance which may cause allergic-type reactions including anaphylactic symptoms or mild to severe asthmatic episodes in certain susceptible persons. Nevertheless, epinephrine is the drug of choice for serious allergic reactions and the presence of a sulfite in this product should not deter administration of the drug for treatment of serious allergic or other emergency situations, even if the patient is sulfite-sensitive. **Reproduction** No studies have been conducted to determine epinephrine's potential effect on fertility. **Special Populations Geriatrics (>65 years of age):** Elderly patients with hypertension, coronary artery disease or cardiac arrhythmias are particularly at risk for epinephrine overdose. More careful monitoring and avoidance of epinephrine overdose is recommended for these patients. **Pediatrics (patients 15-30 kg):** There are no data to suggest a difference in safety or effectiveness of epinephrine between adults and children in this weight group. **Pregnancy:** Although there are no adequate and well-controlled studies in pregnant women, epinephrine should be used in pregnancy only if the potential benefit justifies the potential risk to the fetus.

ADVERSE REACTIONS

Adverse reactions of epinephrine include transient, moderate anxiety; feelings of over stimulation; apprehensiveness; restlessness; tremor; weakness; shakiness; dizziness; sweating; tachycardia; palpitations; pallor; nausea and vomiting; headache; and/or respiratory difficulties. Ventricular arrhythmias may follow administration of epinephrine. While these symptoms occur in some patients treated with epinephrine, they are likely to be more pronounced in patients with hypertension or hypothyroidism. These signs and symptoms usually subside rapidly, especially with bed rest. Some patients may be at greater risk of developing adverse reactions after epinephrine administration. These include elderly individuals, pregnant women, and patients with diabetes. Patients with coronary artery disease are prone to more severe or persistent effects, and may experience angina. Excessive doses cause acute hypertension. Rapid rises in blood pressure have produced cerebral hemorrhage, particularly in elderly patients with cardiovascular disease. Arrhythmias, including fatal ventricular fibrillation, have been reported, particularly in patients with underlying cardiac disease or those receiving certain drugs. The potential for epinephrine to produce these types of adverse reactions does not contraindicate its use in an acute life-threatening allergic reaction.

DRUG INTERACTIONS

There are no known contraindications to the use of epinephrine in a life-threatening allergic reaction. **Drug-Drug Interactions** Epinephrine should be used with caution in patients who are on medications that may sensitize the heart to arrhythmias, e.g., digitalis, diuretics, or anti-arrhythmias. In such patients, epinephrine may precipitate or aggravate angina pectoris as well as produce ventricular arrhythmias. Caution is advised in patients receiving cardiac glycosides or diuretics, since these agents may sensitize the myocardium to beta-adrenergic stimulation and make cardiac arrhythmias more likely. The effects of epinephrine may be potentiated by tricyclic antidepressants, monoamine oxidase inhibitors, sodium levothyroxine, and certain antihistamines, notably chlorpheniramine, triprolenamine, and diphenhydramine. The cardiostimulating and bronchodilating effects of epinephrine are antagonized by beta-adrenergic blocking drugs, such as propranolol. Anaphylaxis may be made worse by beta blockers because these drugs decrease the effectiveness of epinephrine. The vasoconstricting and hypertensive effects of epinephrine are antagonized by alpha-adrenergic blocking drugs, such as phentolamine. Phenothiazines may also reverse the pressor effects of epinephrine. Deaths have been reported in asthmatic patients treated with epinephrine following the use of isoproterenol, orciprenaline, salbutamol, and long acting beta agonists. **Drug-Lifestyle Interactions** Cocaine sensitizes the heart to catecholamines (as does uncontrolled hyperthyroidism), and epinephrine use in these patients should be cautious. To report an adverse event, contact your Regional Adverse Reaction Monitoring Office at 1-866-234-2345 or write to King Pharmaceuticals Canada, Inc., 2915 Argenta Road, Suite 7, Mississauga, Ontario L5N 8G6.



Administration

DOSAGE AND ADMINISTRATION

Dosing Considerations Dosage in any specific patient should be based on body weight. A physician who prescribes EpiPen or EpiPen Jr should take appropriate steps to ensure that the patient thoroughly understands the indications and use of the device. The physician should review with the patient, in detail, the **CONSUMER INFORMATION** section and operation of the Auto-injector. EpiPen and EpiPen Jr contain 2 mL of solution but deliver a single dose of 0.3 mL only, with 1.7 mL remaining in the unit after use. **Inject only into the anterolateral aspect of the thigh. Recommended Dose and Dosage Adjustment EpiPen:** EpiPen delivers a dose of 0.3 mg in 0.3 mL of 1:1000 dilution of epinephrine injection, USP. EpiPen is intended for adults and children who weigh 30 kg or more. **EpiPen Jr:** EpiPen Jr delivers a dose of 0.15 mg in 0.3 mL of 1:2000 dilution of epinephrine injection, USP. EpiPen Jr is intended for children who weigh between 15 kg and 30 kg. Since the dose of epinephrine delivered from EpiPen Jr is fixed at 0.15 mg, the physician can consider other forms of injectable epinephrine if doses lower than 0.15 mg are felt to be necessary (e.g., for children weighing less than 15 kg). **Administration** Patients with a history of severe allergic reactions should be instructed about the circumstances under which epinephrine should be used. The patient's physician or pharmacist should review the package insert in detail with the patient or caregiver to ensure that he/she understands the indications and use of EpiPen or EpiPen Jr. Actual demonstration of the injection technique by a physician or a pharmacist is recommended. A training device for patient instruction purposes is also available. **EpiPen and EpiPen Jr are intended for intramuscular use in the anterolateral aspect of the thigh**, through clothing if necessary. **Do not inject into the buttock.**

Full Prescribing Information available on request. King Pharmaceuticals Canada, Inc., 2915 Argenta Road, Suite 7, Mississauga, Ontario L5N 8G6

Supplemental Product Information

OVERDOSAGE

Epinephrine is rapidly inactivated in the body, and treatment following overdose with epinephrine is primarily supportive. If necessary, pressor effects may be counteracted by rapidly acting vasodilators or alpha-adrenergic blocking drugs. If prolonged hypotension follows such measures, it may be necessary to administer another pressor drug. Overdosage of epinephrine may produce extremely elevated arterial pressure, which may result in cerebrovascular hemorrhage, particularly in elderly patients. Overdosage sometimes also results in extreme pallor and coldness of the skin, metabolic acidosis, and kidney failure. Suitable corrective measures must be taken in such situations. Epinephrine overdosage can also cause transient bradycardia followed by tachycardia, and these may be accompanied by potentially fatal cardiac arrhythmias. Treatment of arrhythmias consists of administration of a beta-adrenergic blocking drug such as propranolol. If an epinephrine overdose induces pulmonary edema that interferes with respiration, treatment consists of a rapidly acting alpha-adrenergic blocking drug and/or intermittent positive-pressure respiration. Premature ventricular contractions may appear within 1 minute after injection and may be followed by multifocal ventricular tachycardia (prefibrillation rhythm). Subsidence of the ventricular effects may be followed by atrial tachycardia and occasionally by atrioventricular block.



© 2010 King Pharmaceuticals Canada, Inc. • 2915 Argenta Road, Suite 7 • Mississauga, Ontario L5N 8G6
Toll-free: 1-877-EPIPEN1 (1-877-374-7361) • Tel: 1-905-812-9911 • Fax: 1-905-812-9916

EpiPen® is a registered trademark of Mylan Inc. licensed exclusively to its wholly-owned subsidiary, Dey Pharma, L.P. of Napa, California, USA.
EPI-09-111E

EPIPEN.ca
(Epinephrine) Auto-Injectors 0.3/0.15mg

Simple to use when it counts.