Prescribing Information

EpiPen®

Sterile epinephrine injection USP

Unidose 0.3 mg epinephrine auto-injector

EpiPen Jr®

Sterile epinephrine injection USP

Unidose 0.15 mg epinephrine auto-injector

Catecholamine/ Sympatomimetic

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EpiPen

Sterile epinephrine injection USP

EpiPen Jr

Sterile epinephrine injection USP

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	All Nonmedicinal Ingredients
Intramuscular Injection injected into anterolateral aspect of the thigh. Do not inject into the buttock.	EpiPen Syringe, Unidose 0.3 mg epinephrine auto-injector; 0.3 mg in 0.3 mL EpiPen Jr Syringe, Unidose 0.15 mg epinephrine auto-injector; 0.15 mg in 0.3 mL	hydrochloric acid sodium chloride sodium metabisulfite water for injection

INDICATIONS AND CLINICAL USE

EpiPen (0.3 mg Epinephrine Injection, USP, 0.3 mg/0.3 mL) and EpiPen Jr (0.15 mg Epinephrine Injection, USP, 0.15 mg/0.3 mL) are indicated for the emergency treatment of severe allergic reactions (anaphylaxis) 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 (see DOSAGE AND ADMINISTRATION section).

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
- idiopathic anaphylaxis

- exercise-induced anaphylaxis
- other allergens

Epinephrine (adrenaline) 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 therapy only and not as a replacement or substitute for subsequent medical or hospital care, nor are they intended to supplant insect venom hyposensitization.

Clinical Signs and Symptoms of Anaphylaxis

Anaphylaxis is a serious, acute, allergic reaction that may cause death.[1] 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.

Symptoms of anaphylaxis may include:

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.

Epinephrine may prove to be lifesaving when used as directed immediately following exposure to an allergen.

Repeat attacks have occurred hours later without additional exposure to the offending allergen.[2-4] Therefore, it is recommended that a patient suffering from an anaphylactic reaction be observed for an appropriate period because of the possibility of either a "biphasic" reaction (a second reaction) or a prolonged reaction.[4] 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 an 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 48 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.

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.

WARNINGS AND PRECAUTIONS

Emergency Treatment

EpiPen and EpiPen Jr. are intended for immediate administration as emergency supportive therapy and are not intended as a substitute for immediate medical care. More than two

sequential doses of epinephrine should only be administered under direct medical supervision. Advise patients when to seek emergency medical assistance for close monitoring of the anaphylactic episode and in the event further treatment is required.

Patients should be instructed to recognize symptoms of systemic allergic reactions and anaphylaxis (see INDICATIONS AND CLINICAL USE).

General

All patients who are prescribed EpiPen and EpiPen Jr should be thoroughly instructed to understand the indications for use and the correct method of administration. It is strongly advised also to educate the patient's immediate associates (e.g. parents, caregivers, teachers) for the correct usage of EpiPen and EpiPen Jr in case support is needed in the emergency situation.

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 auto-injector prescription.

Epinephrine injection 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.

The patient/carer should be informed about the possibility of biphasic anaphylaxis which is characterized by initial resolution followed by recurrence of symptoms from 1 to 48 hours later.

In patients with a thick subcutaneous fat layer, there is risk for epinephrine not reaching the muscle tissue resulting in a suboptimal effect (see ACTION AND CLINICAL PHARMACOLOGY).

Antihistamines and asthma medications must not be used as first line treatment for an anaphylactic reaction.[5]

There is also a risk for adverse reactions after the administration of adrenaline to patients with hyperthyroidism, phaeochromocytoma, severe renal impairment, prostate adenoma, hypercalcaemia, hypokalaemia, and in elderly patients and pregnant women.

Injection-Related Complications

Epinephrine should ONLY be injected into the anterolateral aspect of the thigh.

Do not inject intravenously: Large doses or accidental intravenous injection of epinephrine may result in cerebral hemorrhage due to sharp rise in blood pressure. Rapidly acting vasodilators can counteract the marked pressor effects of epinephrine if there is such inadvertent administration.

Do not inject into buttock: Patients should be advised that EpiPen and EpiPen Jr is not intended for injection into the buttock. Injection into the buttock may not provide effective treatment of anaphylaxis; advise the patient to go immediately to the nearest emergency room for further treatment of anaphylaxis. Additionally, injection into the buttock has been associated with Clostridial infections (gas gangrene).

Do not inject into digits, hands or feet: Since epinephrine is a strong vasoconstrictor, 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.

Hold leg firmly during injection. Lacerations, bent needles, and embedded needles have been reported when EpiPen and EpiPen Jr have been injected into the thigh of young children who are uncooperative and kick or move during an injection. To minimize the risk of injection related injury when administering EpiPen to young children, instruct caregivers to hold the child's leg firmly in place and limit movement prior to and during injection.

Serious Infections at the Injection Site

Rare cases of serious skin and soft tissue infections, including necrotizing fasciitis and myonecrosis caused by Clostridia (gas gangrene), have been reported at the injection site following epinephrine injection for anaphylaxis. *Clostridium* spores can be present on the skin and introduced into the deep tissue with subcutaneous or intramuscular injection. While cleansing with alcohol may reduce presence of bacteria on the skin, alcohol cleansing does not kill *Clostridium* spores. To decrease the risk of *Clostridium* infection, do not inject EpiPen into the buttock. Advise patients to seek medical care if they develop signs or symptoms of infection, such as persistent redness, warmth, swelling, or tenderness, at the epinephrine injection site.

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.

In patients with high intraocular pressure in angle-closure glaucoma, epinephrine dilates the pupil (mydriasis) and produces an acute episode of angle-closure. Epinephrine reduces intraocular pressure in open-angle glaucoma, decreasing aqueous formation and increasing outflow facility.

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 arrythmias 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.

See **DOSAGE AND ADMINISTRATION** section for dosage requirements based on weight.

Pregnancy:

Although there are no adequate and well-controlled studies in pregnant women, epinephrine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Breastfeeding:

There is no information on the presence of epinephrine in human milk, the effects on breastfed infants, or the effects on milk production. It should be used in the same manner in breastfeeding and non-breastfeeding patients.

ADVERSE REACTIONS

Adverse Drug Reaction Overview

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 hyperthyroidism. 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. Cases of takotsubo (stress) cardiomyopathy have been reported in patients treated with epinephrine. Patients with epinephrine-triggered takotsubo cardiomyopathy are predominantly women and are younger than the typical takotsubo cardiomyopathy patient. These events are characterized by rapid onset of symptoms after epinephrine administration and high complication rates, mostly in the form of cardiogenic shock and acute pulmonary edema. The prognosis is however good with complete recovery in most cases.

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 (see **DRUG INTERACTIONS**).

Lacerations, bent needles, and embedded needles have been reported when EpiPen has been injected into the thigh of young children who are uncooperative and kick or move during the injection [see WARNING AND PRECAUTIONS section].

Injection into the buttock has resulted in cases of gas gangrene.

Adverse reactions experienced as a result of accidental injections may include increased heart rate, local reactions including injection site pallor, coldness and hypoesthesia or injury at the injection site resulting in bruising, bleeding, discoloration, erythema or skeletal injury.

Serious Infections at the Injection Site
Rare cases of serious skin and soft tissue infections, including necrotizing fasciitis and myonecrosis caused by Clostridia (gas gangrene), have been reported at the injection site following epinephrine injection in the thigh. Advise patients to seek medical care if they develop signs or symptoms of infection, such as persistent redness, warmth, swelling, or tenderness, at the epinephrine injection site [see WARNINGS AND PRECAUTIONS section]

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

Overview
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-arrhythmics. 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 (MAO-inhibitors) and catechol-O-methyl transferase inhibitors (COMT inhibitors), thyroid hormones, theophylline, oxytocin, parasympatholytics, certain antihistamines (diphenhydramine, chlorpheniramine), levodopa and alcohol.

Epinephrine inhibits the secretion of insulin, thus increasing the blood glucose level. It may be necessary for diabetic patients receiving epinephrine to increase their dosage of insulin or oral hypoglycaemic drugs.

The cardio stimulating and broncho-dilating 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.

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.

Recommended Dose and Dosage Adjustment

The effective dose is usually in the range 0.005-0.01 mg/kg bodyweight.

Adults

The usual dose is 0.3 mg for intramuscular use.

Pediatric population

Usual pediatric dose is 0.01 mg/kg body weight. However, the prescribing physician has the option of prescribing more or less than these amounts based on careful assessment of each individual patient and recognizing the life-threatening nature of reactions for which this is being described. A dosage below 0.15 mg cannot be administered with EpiPen and EpiPen Jr Auto-Injector. The physician should consider other forms of injectable epinephrine if lower doses are felt to be necessary for small children.

Children and adolescents over 30 kg weight:

The usual dose is 0.3 mg for intramuscular use. For these patients EpiPen Auto-Injector containing 0.3 mg epinephrine per dose is available.

Children between 15 kg and 30 kg in weight:

The usual dose is 0.15 mg for intramuscular use. For these patients EpiPen Jr Auto-Injector containing 0.15 mg epinephrine per dose is available.

Children between 7.5 kg and < 15 kg in weight:

For children weighing between 7.5 to < 15 kg the suitability of EpiPen Jr has to be judged individually.

Children below 7.5 kg in weight:

The use in children weighing less than 7.5 kg is not recommended unless in a life-threatening situation and under medical advice.

Administration

EpiPen and EpiPen Jr are for single use.

EpiPen and EpiPen Jr are intended for intramuscular administration into the anterolateral thigh, not the buttock. It is designed to inject through clothing or directly through the skin.

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.

In the absence of clinical improvement or if deterioration occurs after the initial treatment, a second injection with an additional EpiPen or EpiPen Jr auto-injector may be necessary. The repeated injection may be administered 5 – 15 minutes after the first injection. It is recommended

that patients are prescribed two EpiPen or EpiPen Jr auto-injectors which they should carry at all times.

The patient/carer should be informed that following each use of EpiPen and EpiPen Jr auto-injector:

- As EpiPen and EpiPen Jr auto-injectors are designed as emergency treatment only, the patient should be advised when to seek emergency medical assistance for close monitoring of the anaphylactic episode and in the event further treatment is required.
- Conscious patients should preferably lie flat with feet elevated but sit up if they have breathing difficulties. Unconscious patients should be placed on their side in the recovery position.
- It is recommended that the patient should, if possible, remain with another person for at least a four hour period of observation, although this time may vary.

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.

Instruct caregivers to hold the leg of young children firmly in place and limit movement prior to and during injection. Lacerations, bent needles, and embedded needles have been reported when EpiPen and EpiPen Jr have been injected into the thigh of young children who are uncooperative and kick or move during an injection (see WARNINGS AND PRECAUTIONS section).

Patients with a history of severe allergic reactions should be instructed about the circumstances under which epinephrine should be used (see **INDICATIONS AND CLINICAL USE** section).

The physician prescribing an EpiPen or EpiPen Jr auto-injector must ensure that the patient thoroughly understands the indications for use and the correct method of application. Therefore, the patient's physician or pharmacist should discuss the package insert, the correct handling of the auto-injector and possible symptoms of anaphylactic shock in detail with the patient or caregiver. Actual demonstration of the injection technique by a physician or a pharmacist is recommended.

A training device for patient instruction purposes is also available. Instruct patients and/or caregivers to use and practice with the Trainer to familiarize themselves with the use of EpiPen in an allergic emergency.

EpiPen and EpiPen Jr contain 2 mL of solution but deliver **only** a single dose in a volume of 0.3 mL. Approximately 1.7 mL remains in the auto-injector after activation, but is not available for future use and should be discarded.

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.

ACTION AND CLINICAL PHARMACOLOGY

Epinephrine is a catecholamine which stimulates the sympathetic nervous system (both alpha and beta receptors) by which cardiac rate, cardiac output and coronary circulation is raised. Through its action on alpha-adrenergic receptors, epinephrine counters the vasodilation and high vascular permeability that occurs during an anaphylactic reaction that can lead to loss of intravascular fluid volume and hypotension. Through its action on beta-adrenergic receptors, epinephrine causes bronchial smooth muscle relaxation that helps alleviate bronchospasm, wheezing, and dyspnea that may occur during anaphylaxis.

Epinephrine also helps to alleviate pruritus, urticaria, and angioedema, and may be effective in relieving gastrointestinal and genitourinary symptoms of anaphylaxis because of its relaxant effects on the smooth muscle of the stomach, intestine, and urinary bladder. Epinephrine contracts the smooth muscle of the uterus.

Epinephrine is a naturally occurring substance produced by the adrenal medulla and secreted in response to exertion or stress. It is rapidly inactivated in the body mostly by the enzymes COMT

and MAO. The liver is rich in these enzymes and is an important, although not essential, tissue in the degradation process.

Much of the dose of epinephrine is accounted for by excretion of metabolites in the urine. Epinephrine, when given intramuscularly or subcutaneously, has a rapid onset and short duration of action.

Absorption of subcutaneously administered epinephrine is slowed by local vasoconstriction while absorption is more rapid following intramuscular injection due to localized vasodilation.

In a pharmacokinetic study in 35 healthy adult subjects, grouped by varying degrees of thickness in the subcutaneous fat layer of the thigh and stratified by gender, a single 0.3 mg/0.3 ml injection at the anterolateral aspect of the mid-thigh was made with an EpiPen Auto-Injector and was compared in crossover design to a manual syringe-delivered dose with needles individualized for delivery to muscle layer. The results indicate no significant differences between subjects with varying thicknesses of subcutaneous fat layer (<15 mm, ≥15 mm and ≤20 mm, or >20 mm skin to muscle distance under maximum compression). Overall adrenaline exposure from 0 to 30 min ($AUC_{0\text{-}30min}$) for all groups of subjects receiving EpiPen exceeded exposures resulting from syringe delivery. Both inter-subject and intra-subject variability was, however, high in this study and therefore robust conclusions cannot be drawn.

STORAGE AND STABILITY

Shelf-life:
EpiPen: 24 months
EpiPen Jr: 19 months

Always keep EpiPen or EpiPen Jr in the carrier tube to protect it from damage; however, the carrier tube is not waterproof.

Store at 20°C to 25°C, excursions permitted to 15°C-30°C.

Do not refrigerate or freeze.

Protect from light. Keep out of reach and sight of children.

Periodically check to make sure the medicine in the auto-injector is not brown in color. Discard and replace if it is discolored or contains a precipitate.

The expiry date is indicated on the label; EpiPen or EpiPen Jr should not be used after this date. Replace and discard the auto-injector after expiry date.

DOSAGE FORMS, COMPOSITION AND PACKAGING

EpiPen and EpiPen Jr are designed to provide emergency treatment when medical care is not immediately available.

Highly sensitive individuals should have epinephrine injectable products readily available at all times.

EpiPen
Each auto-injector contains: 2 mL epinephrine injection 1 mg/mL and is designed to deliver a single dose of 0.3 mg epinephrine in 0.3 mL.

Nonmedicinal ingredients: Each mL contains: sodium chloride 6 mg, sodium metabisulfite 1.67 mg and hydrochloric acid to adjust pH.

EpiPen Jr
Each auto-injector contains: 2 mL epinephrine injection 0.5 mg/mL and is designed to deliver a single dose of 0.15 mg epinephrine in 0.3 mL.

Nonmedicinal ingredients: Each mL contains: sodium chloride 6 mg, sodium metabisulfite 1.67 mg and hydrochloric acid to adjust pH.

PART II: SCIENTIFIC INFORMATION

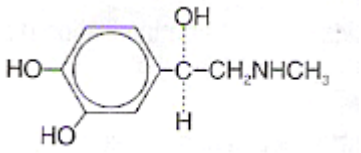
PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: Epinephrine

Chemical name: 1-(3,4-dihydroxyphenyl)-2-(methylamino)ethanol

Structural formula:



Physicochemical properties: Epinephrine is a sympathomimetic catecholamine. Its naturally occurring *l*-isomer, which is twenty times as active as the *d*-isomer, is obtained in pure form by separation from the synthetically produced racemate.

REPRODUCTION

Teratogenic Effects.
Epinephrine has been shown to have adverse developmental effects in rabbits at a subcutaneous dose of 1.2 mg/kg (approximately 30 times the maximum recommended daily subcutaneous or intramuscular dose on a mg/m^2 basis), in mice at a subcutaneous dose of 1 mg/kg (approximately 7 times the maximum recommended daily subcutaneous or intramuscular dose on a mg/m^2 basis), and in hamsters at a subcutaneous dose of 0.5 mg/kg (approximately 5 times the maximum recommended daily subcutaneous or intramuscular dose on a mg/m^2 basis).

These effects were not seen in mice at a subcutaneous dose of 0.5 mg/kg (approximately 3 times the maximum recommended daily subcutaneous or intramuscular dose on a mg/m^2 basis).

REFERENCES

1. Sampson H. et al. Second Symposium on the Definition and Management of Anaphylaxis: Summary Report – Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network Symposium. Journal of Allergy and Clinical Immunology 2006: 117(2) 391-397.

2. Stark BJ, Sullivan TJ. Biphasic and protracted anaphylaxis. Journal of Allergy and Clinical Immunology 1986; 78:76-83.

3. Lieberman P. Biphasic Anaphylaxis (Review) Allergy and Clinical Immunology International – Journal of the World Allergy Organization 2004;16:241-248.

4. Sampson HA. Anaphylaxis and Emergency Treatment. Pediatrics 2003;111;1601-1608

5. Allen, M. et al. (2005) Anaphylaxis in Schools and Other Settings, Hamilton, Ontario: Canadian Society of Allergy and Clinical Immunology.

PART III: CONSUMER INFORMATION

EpiPen®
Sterile epinephrine injection, USP
Unidose 0.3 mg epinephrine Auto-injector

EpiPen Jr®
Sterile epinephrine injection, USP
Unidose 0.15 mg epinephrine Auto-injector

This leaflet is Part III of a three-part "Prescribing Information" document published when EpiPen, EpiPen Jr were approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about EpiPen, EpiPen Jr. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:
EpiPen and EpiPen Jr are indicated for the emergency treatment of severe allergic reactions (anaphylaxis). They are intended for immediate use in patients who are at increased risk for anaphylaxis, including individuals with a history of having anaphylactic reactions.

EpiPen and EpiPen Jr should be used immediately to treat yourself or your child when experiencing a severe allergic reaction. This is emergency treatment. It does not replace seeing a doctor or going to the hospital.

Anaphylaxis is the term for a severe, life-threatening allergic reaction. A severe allergic reaction occurs when a person is exposed to an allergen (an allergy-causing substance). When the allergen enters the body it triggers the releases of chemicals that can lead to life-threatening symptoms.

Some common allergens include:
- foods like peanuts, tree nuts, shellfish, fish, milk, eggs and wheat
- insect stings like those from bees, wasps, hornets, yellow jackets and fire ants
- insect bites like those from mosquitos and black flies
- certain medicines
- latex
- other allergens (a substance that causes allergies)

These severe allergic reactions can also be caused by exercise, asthma or by unknown causes.

Those who are considered to be at a higher risk of anaphylaxis include people:
- who have previously experienced allergic reactions or anaphylaxis
- who suffer from asthma
- who have food allergies

Anaphylaxis affects multiple body systems: skin, upper and lower respiratory system, intestinal tract, heart and blood vessels.

The most common warning symptoms of anaphylaxis are:
- Hives and swelling

Typical symptoms of anaphylaxis include:
- Swelling of the throat, lips, tongue, or the area around the eyes
- Hives
- Difficulty breathing or swallowing
- Wheezing and cough
- Metallic taste or itching in the mouth
- Flushing, itching, or redness of the skin
- Stomach cramps, nausea, vomiting, or diarrhea
- Increased heart rate
- Decreased blood pressure
- Chest pain
- Irregular heartbeat
- Paleness
- Sudden feeling of weakness
- Feeling faint
- Anxiety or an overwhelming sense of doom
- Collapse
- Loss of consciousness

What it does:
EpiPen and EpiPen Jr contain epinephrine, which is the medication that helps to decrease your body's allergic reaction. Some of the ways it works include:
- Relaxing the muscles in your airways so you can breathe more easily
- Helping to reverse the rapid and dangerous decrease in blood pressure
- Relaxing the muscles in your stomach, intestines, and bladder

What the medicinal ingredient is:
Epinephrine.

What the nonmedicinal ingredients are:
Hydrochloric acid, sodium chloride, sodium metabisulfite, and water for injection.

What dosage forms it comes in:
EpiPen: Unidose 0.3 mg epinephrine auto-injector

EpiPen Jr: Unidose 0.15 mg epinephrine auto-injector

EpiPen and EpiPen Jr come in disposable, prefilled automatic injection devices.

EpiPen and EpiPen Jr are single-use injectable devices that deliver a fixed dose of epinephrine.

WARNINGS AND PRECAUTIONS

BEFORE you obtain EpiPen or EpiPen Jr, talk to your doctor or pharmacist about all of your medical conditions, especially if you have:

- heart disease
- irregular heartbeat
- high blood pressure
- diabetes
- thyroid conditions
- narrow-angle glaucoma
- depression or other mental disease
- Parkinson's disease
- severe kidney disease
- a tumor on the adrenal gland
- a tumor in the prostate gland
- very high calcium levels in your blood
- very low potassium levels in your blood
- asthma
- previously had an allergic reaction
- an allergy to any of the ingredients in this medication
- also notify your doctor and pharmacist if you are pregnant or breast feeding

EpiPen or EpiPen Jr is the first line emergency treatment for severe, life-threatening allergic reactions even if you have the above conditions.

Other warnings you should know about:

General: If you had a severe, life-threatening allergic reaction in the past, you are at a higher risk for having one again. You should carry EpiPen or EpiPen Jr with you at all times. You or your child should also wear some form of medical identification bracelet or necklace.

Get emergency medical help for further treatment of the anaphylactic episode after using this medication.

Patients with Asthma: if you or your child has asthma, and it is not controlled properly, you are at a higher risk of having breathing problems when you have a severe allergic reaction.

EpiPen or EpiPen Jr contains metabisulfite. This can cause allergic reactions and bronchospasms in those with a history of asthma. You should follow your doctor's instructions carefully on when you or child can use EpiPen or EpiPen Jr.

Injection site: You should **ONLY** inject EpiPen or EpiPen Jr into the **outer side of your upper thigh - into the muscle** (see Proper Use of this Medication).

Do not inject it into the:

- vein (intravenously (IV))
- buttocks
- hands, fingers, feet and toes

If you do, it can either cause dangerously high blood pressure or you or your child may not get the effect of the emergency treatment that you or they need.

If you accidentally inject it into any of these areas, **go right away** to the nearest hospital (emergency room) for further treatment.

If you inject a young child with EpiPen or EpiPen Jr hold their leg firmly in place and limit movement before and during the injection to prevent injuries. Ask your healthcare provider to show you how to properly hold the leg of a young child during injection.

If you have a thick layer of fat under your skin the epinephrine in EpiPen or EpiPen Jr may not reach your muscle tissue. In some cases this might make EpiPen and EpiPen Jr not work as well.

INTERACTIONS WITH THIS MEDICATION

Drugs that may interact with EpiPen or EpiPen Jr include:

- Heart rhythm medicine, such as digoxin or quinidine (another name for digoxin is digitalis)
- Diuretic medicines ("water pills")
- MAO inhibitors (MAOI), such as selegiline, isocarboxazid, phenelzine sulfate, or tranylcypromine
- Tricyclic antidepressants, such as amitriptyline, doxepin, nortriptyline
- Antihistamines, such as chlorpheniramine, tripelennamine, or diphenhydramine
- Beta-adrenergic blocking drugs, such as propranolol
- Alpha-adrenergic blocking drugs, such as phentolamine
- Ergot alkaloids and phenothiazines
- Isoproterenol, orciprenaline, salbutamol and LABAs
- Thyroid medications (e.g. sodium levothyroxine)
- Cocaine
- Theophylline, used to treat types of lung diseases
- Oxytocin, used during labour
- Parasympatholytic medications, used to reduce activity of the nervous system
- Levodopa, used in the treatment of Parkinson's disease
- Alcohol

PROPER USE OF THIS MEDICATION

If you have been told by your doctor that you are at risk for an anaphylactic reaction, carry your EpiPen or EpiPen Jr with you at all times.

When your doctor prescribes EpiPen or EpiPen Jr, you must make sure you understand the reason it has been prescribed for you. You should be confident that you know exactly how and when to use this medication.

Use EpiPen or EpiPen Jr exactly how your doctor or pharmacist has told you. Ask to have the instructions repeated to you if you are unsure about how to use it. It is recommended that your

family members, carers or teachers are also instructed in the correct use of EpiPen or EpiPen Jr.

There is a training device (Trainer) which you can use to practice. If you have been stung by an insect, try to remove the stinger with your fingernails. Do not squeeze, pinch or push the stinger deeper into the skin. If possible, put an ice pack on the area of the sting. Keep yourself warm and avoid exercise.

For allergic reactions caused by foods make sure you remove any remaining food from the mouth immediately.

IMPORTANT NOTE:

Severe, life-threatening allergic reactions (anaphylaxis) can result in death if not treated immediately.

Talk to your doctor about the warning signs and symptoms of anaphylaxis and when to use EpiPen or EpiPen Jr.

Inject EpiPen or EpiPen Jr **right away** if you experience any of the symptoms of a severe allergic reaction, such as swelling of the throat, lips, tongue or around the eyes, trouble breathing or swallowing.

If you or your child does not feel better or get worse you can inject another dose of EpiPen or EpiPen Jr 5 to 15 minutes after the first injection.

Do not inject more than 2 injections right after each other.

<u>Usual dose:</u>

EpiPen (0.3 mg) should be used for adults and children weighing 30 kg or more.

EpiPen Jr (0.15 mg) should be used for children weighing between 15 kg to 30 kg. For children weighing less than 15 kg, call 911.

Directions for Use

Caution

- Remove EpiPen or EpiPen Jr from carrier tube before use
- Never put thumb, fingers or hand over orange needle end
- Never press or push orange needle end with thumb, fingers, or hand
- The injection needle comes out of orange needle end
- Do not remove blue safety top until ready to use
- Remove blue safety top by pulling straight up (Do not bend or twist off the blue safety top)

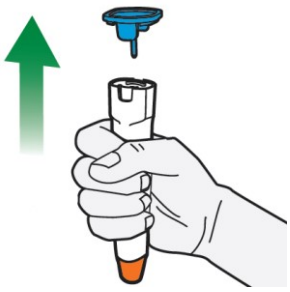
To Take EpiPen or EpiPen Jr out of the Carrier Tube

1. Flip open the cap on the carrier tube. The cap is yellow on EpiPen, green on EpiPen Jr.

2. Tip the carrier tube and slide EpiPen or EpiPen Jr out of the tube.

To Use EpiPen or EpiPen Jr

1. Grasp EpiPen or EpiPen Jr with the orange needle end pointing downward, form a fist around the unit [orange needle end down], pull off blue safety top. (Do not bend or twist off the blue safety top.)



2. Place the orange needle end against the middle of the outer thigh (upper leg) at a right angle to the thigh. Push hard against leg. The pop signals that the injection has started. After pop, hold firmly in place for 3 seconds (count slowly, '1, 2, 3'). Inject even through clothing if necessary. Do not inject EpiPen or EpiPen Jr into your hands, feet, or buttock.

3. Remove EpiPen or EpiPen Jr from the thigh. Massage the injected area if desired. **Note**: The orange needle cover automatically extends to cover the injection needle when EpiPen or EpiPen Jr is removed from the thigh. If the needle is still visible, do not attempt to reuse it.

4. The injection is now complete.

5. If you are administering EpiPen or EpiPen Jr to a young child, hold the leg firmly in place while administering the injection.

6. The effects of epinephrine can wear off and there is a chance of a second reaction. Get emergency medical help for further treatment of the anaphylactic episode after using this medication. With a severe, long-lasting allergic reaction, you may need to administer an additional dose of epinephrine. More than two sequential doses of epinephrine should only be administered under direct medical supervision.

The used EpiPen or EpiPen Jr with extended orange needle cover will not fit back into the carrier. Give any used EpiPen or EpiPen Jr to emergency responders or emergency room personnel.

Do not attempt to reuse EpiPen after the device has been activated.

Overdose:

If you take more than the recommended dose, or inject the EpiPen or EpiPen Jr anywhere other than your thigh, contact a healthcare professional, hospital emergency department, regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669) immediately, even if there are no signs or symptoms.

Too much epinephrine can cause dangerously high blood pressure, stroke, or death.

Signs of an overdose include:

- irregular heart beat
- difficulty breathing caused by a build-up of fluid in your lungs

SERIOUS SIDE EFFECTS AND WHAT TO DO ABOUT THEM

EpiPen and EpiPen Jr are intended to be used immediately to treat yourself or your child when suffering from a severe allergic reaction. This is emergency treatment that may prove to be lifesaving when used as directed.

After you use EpiPen or EpiPen Jr always seek appropriate medical care.

The following side effects may occur after using EpiPen or EpiPen Jr.

- Paleness
- Dizziness
- Weakness
- Shaking
- Headache
- Throbbing
- Restlessness
- Anxiety
- Tenseness
- Fear
- Feeling cold

Patients who have used EpiPen or EpiPen Jr may develop infections at the injection site within a few days of an injection. Some of these infections can be serious. Call your healthcare provider right away if you have any of the following at an injection site:

- redness that does not go away
- swelling
- tenderness
- the area feels warm to the touch

Cuts on the skin, bent needles, and needles that remain in the skin after the injection, have happened in young children who do not cooperate and kick or move during an injection.

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
Difficulty breathing			✓
Increased heart rate (pounding heart)			✓
Irregular or skipped heart beats			✓
Chest pain (angina)			✓
Stroke (blurred vision, difficulty speaking,			✓

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
headache, dizziness and weakness)			

This is not a complete list of side effects. For any unexpected effects while taking EpiPen or EpiPen Jr, talk to your doctor or pharmacist.

Get emergency medical help for further treatment of the anaphylactic episode after using this medication.

HOW TO STORE IT

- Keep your EpiPen or EpiPen Jr at 20°C – 25°C, excursions permitted to 15°C – 30°C. Do not refrigerate or freeze. Do not drop.
- Do not expose your EpiPen or EpiPen Jr to direct sunlight. Keep out of reach and sight of children.
- Do not keep your EpiPen or EpiPen Jr in a vehicle during extremely hot or cold weather.
- Always keep your EpiPen or EpiPen Jr in the carrier tube to protect it from damage; however, the carrier tube is not waterproof.
- The blue safety top helps to prevent accidental injection. Keep the blue safety top on until you need to use EpiPen or EpiPen Jr.
- Occasionally inspect your EpiPen or EpiPen Jr medicine through the viewing window. Replace your EpiPen or EpiPen Jr if it is discolored or contains solid particles (precipitate) or if there are any signs of leakage. The medicine should be clear.
- Discard if there are any signs of damage to the carrier or the EpiPen or EpiPen Jr.
- Do not attempt to take the EpiPen or EpiPen Jr apart. Replace your EpiPen or EpiPen Jr before the expiration date or after you use it.
- Talk to your pharmacist or physician about how to properly dispose of your expired EpiPen or EpiPen Jr.
- Do not place this Consumer Information or any other objects in the carrier tube with your EpiPen or EpiPen Jr, as this may prevent you from removing your EpiPen or EpiPen Jr quickly for use.
- Keep out of the reach and sight of children.

Reporting Side Effects
You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (canada.ca/drug-device-reporting) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your healthcare professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

EXPIRATION REMINDER SERVICE

Patients may also register the expiration date of their EpiPen, EpiPen Jr at www.EpiPen.ca. Shortly before this emergency care product expires patients will be notified by E-mail or text message that the product is nearing expiry and should be replaced.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at: www.EpiPen.ca or by contacting BGP Pharma ULC 1-877-EPIPEN 1 (1-877-374-7361).

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