

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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Date of Revision:
May 30, 2017

Submission Control No: 205110

Table of Contents

PART I: HEALTH PROFESSIONAL INFORMATION.....	3
SUMMARY PRODUCT INFORMATION	3
INDICATIONS AND CLINICAL USE.....	3
CONTRAINDICATIONS	6
WARNINGS AND PRECAUTIONS.....	6
ADVERSE REACTIONS.....	9
DRUG INTERACTIONS	10
DOSAGE AND ADMINISTRATION.....	11
OVERDOSAGE	13
ACTION AND CLINICAL PHARMACOLOGY	13
STORAGE AND STABILITY.....	14
DOSAGE FORMS, COMPOSITION AND PACKAGING	14
PART II: SCIENTIFIC INFORMATION	16
PHARMACEUTICAL INFORMATION.....	16
REPRODUCTION.....	16
REFERENCES	17
PART III: CONSUMER INFORMATION.....	18

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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 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 (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 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.

Clinical Signs and Symptoms of Anaphylaxis

Anaphylaxis is a serious, acute, allergic reaction that may cause death¹. 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.

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.²⁻⁴ 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.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 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.

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. **In conjunction with the administration of epinephrine, the patient should seek immediate medical or hospital care.** More than two sequential doses of epinephrine should only be administered under direct medical supervision.

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 characterised by initial resolution followed by recurrence of symptoms some hours later.

In patients with a thick subcutaneous fat layer, there is risk for adrenaline not reaching the muscle tissue resulting in a suboptimal effect.

Antihistamines and asthma medications must not be used as first line treatment for an anaphylactic reaction⁵.

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.

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.

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.

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.

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 in pregnancy only if the potential benefit justifies the potential risk to the fetus.

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.

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, sodium levothyroxine, and certain antihistamines, notably chlorpheniramine, triproleamine, and diphenhydramine.

The cardiostimulating and bronchodilating effects of epinephrine are antagonized by betaadrenergic 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 alphaadrenergic 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.

EpiPen[®]:

The EpiPen[®] auto-injector is intended for intramuscular administration in adults and children who weigh 30 kg or more.

EpiPen[®] auto-injector delivers a single intramuscular dose of 0.3 mg epinephrine in a 0.3 mL volume (0.3 mg/0.3 mL).

EpiPen Jr[®]:

The EpiPen Jr[®] auto-injector is intended for pediatric intramuscular administration in children who weigh between 15 kg and 30 kg.

EpiPen Jr[®] auto-injector delivers a single intramuscular dose of 0.15 mg epinephrine in a 0.3 mL volume (0.15 mg/0.3 mL).

For children weighing more than 30 kg, EpiPen[®] auto-injector 0.3 mg (adult formulation) is recommended.

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

An initial dose should be administered as soon as symptoms of anaphylaxis are recognised. In the absence of clinical improvement or if deterioration occurs after the initial treatment, a second injection with an additional EpiPen[®] auto-injector 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.

All individuals receiving emergency epinephrine must be immediately transported to hospital, ideally by ambulance, for evaluation and observation even if symptoms appear to be improving.

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

- As EpiPen[®] and EpiPen Jr[®] auto-injector is designed as emergency treatment only, the patient should be advised to always seek medical help immediately.
- 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.
- The patient should if possible remain with another person until medical assistance arrives.

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).

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 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. 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, with 1.7 mL remaining in the unit **after use**.

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 acts on both alpha- and beta-adrenergic receptors. 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, when given intramuscularly or subcutaneously, has a rapid onset and short duration of action.

STORAGE AND STABILITY

Shelf-life:

EpiPen[®]: 20 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 25°C (77°F); EXCURSIONS PERMITTED TO 15° - 30°C (59 ° - 86°F).

Do not refrigerate or freeze.

Protect from light.

Periodically check to make sure the solution 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

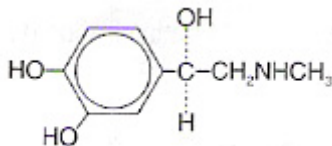
PHARMACEUTICAL INFORMATION

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. Pregnancy Category C

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/m² 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/m² 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/m² 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/m² 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 anaphylaxis and are intended for people determined to be at risk for serious allergic reactions and for people with a history of 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 heart beat
- 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 have 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.

Using EpiPen® or EpiPen Jr® does not replace seeing a doctor or going to the hospital. You **must** get medical help **right away** after you or your child has used it.

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 tranlycypromine
- Tricyclic antidepressants, such as amitriptyline, doxepin, nortriptyline
- Antihistamines, such as chlorpheniramine, tripelemnamine, 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

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 it.

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. You **must** get medical help **right away** after using EpiPen® or EpiPen Jr®. You can:

- call 911 and get taken to the hospital OR
- you can have someone take you (or you can take your child) to the nearest hospital emergency room

If you or your child do 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.

Usual dose:

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 tip
- Never press or push orange tip with thumb, fingers, or hand
- The injection needle comes out of orange tip
- Do not remove blue safety release cap until ready to use
- Remove blue safety release cap by pulling straight up (Do not bend or twist off the blue safety release cap)

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®.

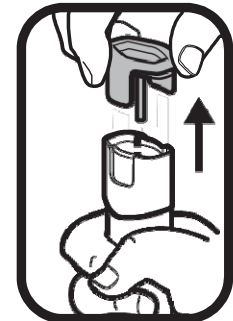


2. Tip the carrier tube and slide EpiPen® or EpiPen Jr® out of the tube.



To Use EpiPen® or EpiPen Jr®

1. Grasp EpiPen® or EpiPen Jr® with the orange tip pointing downward, form a fist around the unit [orange tip (needle end) down], remove blue safety release cap by pulling straight up. (Do not bend or twist off the blue safety release cap.)



- Place the orange tip against the middle of the outer thigh (upper leg) at a right angle to the thigh. Swing and push the auto-injector firmly until it “clicks”. The click signals that the injection has started. 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.



- 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.



- The injection is now complete.
- If you are administering EpiPen® or EpiPen Jr® to a young child, hold the leg firmly in place while administering the injection.
- Seek medical attention immediately even if the severe allergy symptoms seem to have subsided. Because the effects of epinephrine can wear off and there is a chance of a second reaction, **it is important that you seek medical assistance or go to the emergency room immediately after using EpiPen® or EpiPen Jr®.**
- Even if you have sought medical help, you must stay within close proximity to a hospital or where you can easily call 911 for the next 48 hours.**

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 your healthcare professional, hospital emergency department or regional Poison Control Centre immediately, even if there are no 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.

After you use EpiPen® or EpiPen Jr® always seek appropriate medical care. EpiPen® or EpiPen Jr® does not replace seeing a doctor or going to the hospital.

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

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

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, 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.

It is important that you seek medical assistance or go to the emergency room immediately after using EpiPen® or EpiPen Jr®.

HOW TO STORE IT

- Keep your EpiPen® or EpiPen Jr® at room temperature. Do not refrigerate. Do not drop.
- Do not expose your EpiPen® or EpiPen Jr® to direct sunlight.
- 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 release cap helps to prevent accidental injection. Keep the blue safety release cap on until you need to use EpiPen® or EpiPen Jr®.
- Occasionally inspect your EpiPen® or EpiPen Jr® solution 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 solution 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 (<http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health 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 Pfizer Canada Inc. 1-877-EPIPEN 1 (1-877-374-7361).

This leaflet was prepared by Mylan Specialty L.P.

Manufactured for Mylan Specialty L.P., Morgantown, WV 26505, U.S.A. by Meridian Medical Technologies®, Inc., Columbia, MD 21046, U.S.A. Distributed in Canada by Pfizer Canada Inc., Kirkland, Quebec, H9J 2M5.

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Last revised: May 30, 2017

MS:EPICE:R1 • 00111-11-2E • 0002002