

EPIPEN®**EPIPEN Jr®**

(epinephrine injection, USP) Auto-Injectors 0.3/0.15mg

EpiPen® Auto-Injector: The #1 prescribed brand for 25+ years*

Over the years, doctors have prescribed EpiPen® Auto-Injector more than any other brand of epinephrine auto-injector for those at increased risk for anaphylaxis.* Anaphylaxis (an-a-fi-lax-is) is the medical term for a life-threatening allergic reaction. It can occur within minutes after your immune system mistakenly overreacts to an allergen. Know what symptoms to look for.

DO YOU KNOW THE SIGNS AND SYMPTOMS OF ANAPHYLAXIS?

MOUTH

- Itching
- Swelling of lips and/or tongue

LUNGS

- Shortness of breath
- Coughing
- Wheezing

SKIN

- Itching
- Hives
- Redness
- Swelling

THROAT

- Itching
- Tightness/closure
- Coughing

HEART

- Weak pulse
- Dizziness
- Passing out

STOMACH

- Vomiting
- Nausea
- Diarrhea
- Cramps



*Based on IMS data from 1987-May 2016.

WHAT CAUSES ANAPHYLAXIS?

Anaphylaxis can be triggered by a number of allergens, including:



PEANUTS



TREE NUTS



MILK



EGGS



SHELLFISH



FISH



WHEAT



SOY



STINGING INSECTS



MEDICATIONS



LATEX



EXERCISE

LIFE HAPPENS. Be Prepared.®

Being prepared means having a plan to:

- Avoid known allergens
- Know what symptoms to watch for
- Use an EpiPen® (epinephrine injection, USP) Auto-Injector if a life-threatening allergic reaction occurs
- Get emergency medical help right away

IMPORTANT SAFETY INFORMATION

Use EpiPen® (epinephrine injection, USP) 0.3 mg or EpiPen Jr® (epinephrine injection, USP) 0.15 mg Auto-Injectors right away when you have an allergic emergency (anaphylaxis).

Get emergency medical help right away. You may need further medical attention. Only a healthcare professional should give additional doses of epinephrine if you need more than two injections for a single anaphylactic episode. EpiPen® or EpiPen Jr® should only be injected into the middle of your outer thigh (upper leg), through clothing if necessary. Do not inject into your veins, buttocks, fingers, toes, hands or feet. Hold the leg of young children firmly in place before and during injection to prevent injuries. In case of accidental injection, please seek immediate medical treatment.

Rarely, patients who have used EpiPen® or EpiPen Jr® may develop an infection at the injection site within a few days. Some of these infections can be serious. Call your healthcare professional right away if you have any of the following at an injection site: redness that does not go away, swelling, tenderness, or the area feels warm to the touch.

Tell your healthcare professional about all of your medical conditions, especially if you have asthma, a history of depression, thyroid problems, Parkinson's disease, diabetes, high blood pressure or heart problems, have any other medical conditions, are pregnant or plan to become pregnant, or are breastfeeding or plan to breastfeed. Be sure to also tell your healthcare professional all the medicines you take, especially medicines for asthma. **If you have certain medical conditions, or take certain medicines, your condition may get worse or you may have longer lasting side effects when you use EpiPen® or EpiPen Jr®.**

Only a healthcare professional can assess the risk of having a life-threatening allergic reaction (anaphylaxis). This information is provided for your education and is not a substitute for diagnosis by a healthcare professional.

For more information, visit epipen.com.

IMPORTANT SAFETY INFORMATION (CONTINUED)

Common side effects include fast, irregular or "pounding" heartbeat, sweating, nausea or vomiting, breathing problems, paleness, dizziness, weakness, shakiness, headache, feelings of over excitement, nervousness or anxiety. These side effects usually go away quickly if you lie down and rest. **Tell your healthcare professional if you have any side effect that bothers you or that does not go away.**

Please see accompanying full Prescribing Information and Patient Information.

INDICATIONS

EpiPen® and EpiPen Jr® Auto-Injectors are for the emergency treatment of life-threatening allergic reactions (anaphylaxis) caused by allergens, exercise, or unknown triggers; and for people who are at increased risk for these reactions. EpiPen® and EpiPen Jr® are intended for immediate administration as emergency supportive therapy only. Seek immediate emergency medical help right away.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

For additional information, please contact us at 800-395-3376.

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use **EPIPEN®** and **EPIPEN Jr®** safely and effectively. See full prescribing information for **EPIPEN®** and **EPIPEN Jr®**.

EPIPEN® (epinephrine injection, USP), Auto-Injector 0.3 mg, **EPIPEN Jr®** (epinephrine injection, USP) Auto-Injector 0.15 mg, for intramuscular or subcutaneous use
Initial U.S. Approval: 1939

RECENT MAJOR CHANGES

- Dosage and Administration (2) 05/2016
- Warnings and Precautions (5.2, 5.3) 05/2016

INDICATIONS AND USAGE

EpiPen® and EpiPen Jr® contain epinephrine, a non-selective alpha and beta-adrenergic receptor agonist, indicated in the emergency treatment of allergic reactions (Type I) including anaphylaxis. (1)

DOSAGE AND ADMINISTRATION

- Patients greater than or equal to 30 kg (66 lbs): EpiPen® 0.3 mg (2)
- Patients 15 to 30 kg (33 lbs to 66 lbs): EpiPen Jr® 0.15 mg (2)

Inject EpiPen® and EpiPen Jr® intramuscularly or subcutaneously into the anterolateral aspect of the thigh, through clothing if necessary. Each device is a single-use injection. (2)

DOSAGE FORMS AND STRENGTHS

- EpiPen®: Injection, 0.3 mg: 0.3 mg/0.3 mL epinephrine, USP, pre-filled auto-injector (3)
- EpiPen Jr®: Injection, 0.15 mg: 0.15 mg/0.3 mL epinephrine, USP, pre-filled auto-injector (3)

CONTRAINDICATIONS

None (4)

WARNINGS AND PRECAUTIONS

- In conjunction with use, seek immediate medical or hospital care. (5.1)
- Do not inject intravenously, into buttock, or into digits, hands, or feet. (5.2)
- To minimize the risk of injection related injury, instruct caregivers to hold the child's leg firmly in place and limit movement prior to and during injection when administering to young children. (5.2)
- Rare cases of serious skin and soft tissue infections have been reported following epinephrine injection. Advise patients to seek medical care if they develop signs or symptoms of infection. (5.3)
- The presence of a sulfite in this product should not deter use. (5.4)
- Administer with caution in patients with heart disease; may aggravate angina pectoris or produce ventricular arrhythmias. (5.5)

ADVERSE REACTIONS

Adverse reactions to epinephrine include anxiety, apprehensiveness, restlessness, tremor, weakness, dizziness, sweating, palpitations, pallor, nausea and vomiting, headache, and/or respiratory difficulties. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Mylan Specialty, L.P. at 1-877-446-3679 (1-877-4-INFO-RX) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Cardiac glycosides or diuretics: observe for development of cardiac arrhythmias. (7)
- Tricyclic antidepressants, monoamine oxidase inhibitors, levothyroxine sodium, and certain antihistamines: potentiate effects of epinephrine. (7)
- Beta-adrenergic blocking drugs: antagonize cardiostimulating and bronchodilating effects of epinephrine. (7)
- Alpha-adrenergic blocking drugs: antagonize vasoconstricting and hypertensive effects of epinephrine. (7)
- Ergot alkaloids: may reverse the pressor effects of epinephrine. (7)

USE IN SPECIFIC POPULATIONS

- Elderly patients may be at greater risk of developing adverse reactions. (5.5, 8.5)

See 17 for PATIENT COUNSELING INFORMATION and FDA approved patient labeling
Revised: May 2016

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*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

EpiPen® and EpiPen Jr® are indicated in the emergency treatment of allergic reactions (Type I) including anaphylaxis to stinging insects (e.g., order Hymenoptera, which include bees, wasps, hornets, yellow jackets and fire ants) and biting insects (e.g., triatoma, mosquitoes), allergen immunotherapy, foods, drugs, diagnostic testing substances (e.g., radiocontrast media) and other allergens, as well as idiopathic anaphylaxis or exercise-induced anaphylaxis. EpiPen® and EpiPen Jr® are intended for immediate administration in patients who are determined to be at increased risk for anaphylaxis, including individuals with a history of anaphylactic reactions.

Anaphylactic reactions may occur within minutes after exposure and consist of flushing, apprehension, syncope, tachycardia, thready or unobtainable pulse associated with a fall in blood pressure, convulsions, vomiting, diarrhea and abdominal cramps, involuntary voiding, wheezing, dyspnea due to laryngeal spasm, pruritus, rashes, urticaria or angioedema.

EpiPen® and EpiPen Jr® are intended for immediate administration as emergency supportive therapy only and are not a substitute for immediate medical care.

2 DOSAGE AND ADMINISTRATION

Selection of the appropriate dosage strength (EpiPen® 0.3 mg or EpiPen Jr® 0.15 mg) is determined according to patient body weight.

- Patients greater than or equal to 30 kg (approximately 66 pounds or more): EpiPen® 0.3 mg
 - Patients 15 to 30 kg (33 pounds to 66 pounds): EpiPen Jr® 0.15 mg
- Inject EpiPen® or EpiPen Jr® intramuscularly or subcutaneously into the anterolateral aspect of the thigh, through clothing if necessary. Instruct caregivers of young children who are prescribed an EpiPen® or EpiPen Jr® and who may be uncooperative and kick or move during an injection to hold the leg firmly in place and limit movement prior to and during an injection [see *Warnings and Precautions* (5.2)]. Each EpiPen® or EpiPen Jr® contains a single dose of epinephrine for single-use injection. Since the doses of epinephrine delivered from EpiPen® or EpiPen Jr® are fixed, consider using other forms of injectable epinephrine if doses lower than 0.15 mg are deemed necessary.
- The prescriber should carefully assess each patient to determine the most appropriate dose of epinephrine, recognizing the life-threatening nature of the reactions for which this drug is indicated. With severe persistent anaphylaxis, repeat injections with an additional EpiPen® or EpiPen Jr® may be necessary. More than two sequential doses of epinephrine should only be administered under direct medical supervision [see *Warnings and Precautions* (5.1)]. The epinephrine solution in the clear window of the EpiPen® Auto-Injector should be inspected visually for particulate matter and discoloration. Epinephrine is light sensitive and should be stored in the carrier tube provided to protect it from light [see *How Supplied/Storage and Handling* (16.2)].

3 DOSAGE FORMS AND STRENGTHS

- EpiPen®: Injection, 0.3 mg/0.3 mL epinephrine injection, USP, pre-filled auto-injector
- EpiPen Jr®: Injection, 0.15 mg/0.3 mL, epinephrine injection, USP, pre-filled auto-injector

4 CONTRAINDICATIONS

None

5 WARNINGS AND PRECAUTIONS

5.1 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 [see *Indications and Usage* (1), *Dosage and Administration* (2) and *Patient Counseling Information* (17)].

5.2 Injection-Related Complications

EpiPen® and EpiPen Jr® should **only** be injected into the anterolateral aspect of the thigh [see *Dosage and Administration* (2) and *Patient Counseling Information* (17)].

- **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.** 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). Cleansing with alcohol does not kill bacterial spores, and therefore, does not lower this risk.
- **Do not inject into digits, hands or feet.** Since epinephrine is a strong vasoconstrictor, accidental injection into the digits, hands or feet may result in loss of blood flow to the affected area. Advise the patient to go immediately to the nearest emergency room and to inform the healthcare provider in the emergency room of the location of the accidental injection. Treatment of such inadvertent administration should consist of vasodilation, in addition to further appropriate treatment of anaphylaxis [see *Adverse Reactions* (6)].
- **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.

5.3 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 [see *Warnings and Precautions* (5.2)]. 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.

5.4 Allergic Reactions Associated With Sulfite

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.

Epinephrine is the preferred treatment for serious allergic reactions or other emergency situations even though this product contains sodium metabisulfite, a sulfite that may, in other products, cause allergic-type reactions including anaphylactic symptoms or life-threatening or less severe asthmatic episodes in certain susceptible persons.

The alternatives to using epinephrine in a life-threatening situation may not be satisfactory.

5.5 Disease Interactions

Some patients may be at greater risk for developing adverse reactions after epinephrine administration. Despite these concerns, it should be recognized that the presence of these conditions is not a contraindication to epinephrine administration in an acute, life-threatening situation. Therefore, patients with these conditions, and/or any other person who might be in a position to administer EpiPen® or EpiPen Jr® to a patient experiencing anaphylaxis should be carefully instructed in regard to the circumstances under which epinephrine should be used.

- Patients with Heart Disease
Epinephrine should be administered with caution to patients who have heart disease, including patients with cardiac arrhythmias, coronary artery or organic heart disease, or hypertension. In such patients, or in patients who are on drugs that may sensitize the heart to arrhythmias, epinephrine may precipitate or aggravate angina pectoris as well as produce ventricular arrhythmias [see *Drug Interactions* (7) and *Adverse Reactions* (6)].
- Other Patients and Diseases

Epinephrine should be administered with caution to patients with hyperthyroidism, diabetes, elderly individuals, and pregnant women. Patients with Parkinson's disease may notice a temporary worsening of symptoms.

6 ADVERSE REACTIONS

Due to the lack of randomized, controlled clinical trials of epinephrine for the treatment of anaphylaxis, the true incidence of adverse reactions associated with the systemic use of epinephrine is difficult to determine. Adverse reactions reported in observational trials, case reports, and studies are listed below. Common adverse reactions to systemically administered epinephrine include anxiety; apprehensiveness; restlessness; tremor; weakness; dizziness; sweating; palpitations; pallor; nausea and vomiting; headache; and/or respiratory difficulties. These symptoms occur in some persons receiving therapeutic doses of epinephrine, but are more likely to occur in patients with hypertension or hyperthyroidism [see *Warnings and Precautions* (5.5)]. Arrhythmias, including fatal ventricular fibrillation, have been reported, particularly in patients with underlying cardiac disease or those receiving certain drugs [see *Warnings and Precautions* (5.5) and *Drug Interactions* (7)]. Rapid rises in blood pressure have produced cerebral hemorrhage, particularly in elderly patients with cardiovascular disease [see *Warnings and Precautions* (5.5)]. Angina may occur in patients with coronary artery disease [see *Warnings and Precautions* (5.5)].

Rare cases of stress cardiomyopathy have been reported in patients treated with epinephrine.

Accidental injection into the digits, hands or feet may result in loss of blood flow to the affected area [see *Warnings and Precautions* (5.2)]. Adverse events 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.

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* (5.2)].

Injection into the buttock has resulted in cases of gas gangrene [see *Warnings and Precautions* (5.2)].

Rare cases of serious skin and soft tissue infections, including necrotizing fasciitis and myonecrosis caused by Clostridia (gas gangrene), have been reported following epinephrine injection, including EpiPen®, in the thigh [see *Warnings and Precautions* (5.3)].

7 DRUG INTERACTIONS

Patients who receive epinephrine while concomitantly taking cardiac glycosides, diuretics, or anti-arrhythmics should be observed carefully for the development of cardiac arrhythmias [see *Warnings and Precautions* (5.5)]. The effects of epinephrine may be potentiated by tricyclic antidepressants, monoamine oxidase inhibitors, levothyroxine sodium, and certain antihistamines, notably chlorpheniramine, tripeleminamine, and diphenhydramine. The cardiostimulating and bronchodilating effects of epinephrine are antagonized by beta-adrenergic blocking drugs, such as propranolol. The vasoconstricting and hypertensive effects of epinephrine are antagonized by alpha-adrenergic blocking drugs, such as phentolamine. Ergot alkaloids may also reverse the pressor effects of epinephrine.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Teratogenic Effects: *Pregnancy Category C.*

There are no adequate and well controlled studies of the acute effect of epinephrine in pregnant women.

Epinephrine was teratogenic in rabbits, mice and hamsters. Epinephrine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus (fetal anoxia, spontaneous abortion, or both). Epinephrine has been shown to have teratogenic effects when administered subcutaneously in rabbits at approximately 30 times the maximum recommended daily subcutaneous or intramuscular dose (on a mg/m² basis at a maternal dose of 1.2 mg/kg/day for two to three days), in mice at approximately 7 times the maximum daily subcutaneous or intramuscular dose (on a mg/m² basis at a maternal subcutaneous dose of 1 mg/kg/day for 10 days), and in hamsters at approximately 5 times the maximum recommended daily subcutaneous or intramuscular dose (on a mg/m² basis at a maternal subcutaneous dose of 0.5 mg/kg/day for 4 days). These effects were not seen in mice at approximately 3 times the maximum recommended daily subcutaneous or intramuscular dose (on a mg/m² basis at a subcutaneous maternal dose of 0.5 mg/kg/day for 10 days).

8.3 Nursing Mothers

It is not known whether epinephrine is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when EpiPen® is administered to a nursing woman.

8.4 Pediatric Use

EpiPen® or EpiPen Jr® may be administered to pediatric patients at a dosage appropriate to body weight [see *Dosage and Administration* (2)]. Clinical experience with the use of epinephrine suggests that the adverse reactions seen in children are similar in nature and extent to those both expected and reported in adults. Since the doses of epinephrine delivered from EpiPen® and EpiPen Jr® are fixed, consider using other forms of injectable epinephrine if doses lower than 0.15 mg are deemed necessary.

8.5 Geriatric Use

Clinical studies for the treatment of anaphylaxis have not been performed in subjects aged 65 and over to determine whether they respond differently from younger subjects. However, other reported clinical experience with use of epinephrine for the treatment of anaphylaxis has identified that geriatric patients may be particularly sensitive to the effects of epinephrine. Therefore, EpiPen® should be administered with caution in elderly individuals, who may be at greater risk for developing adverse reactions after epinephrine administration [see *Warnings and Precautions* (5.5), *Overdosage* (10)].

10 OVERDOSAGE

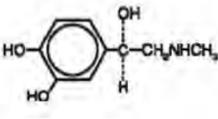
Overdosage of epinephrine may produce extremely elevated arterial pressure, which may result in cerebrovascular hemorrhage, particularly in elderly patients. Overdosage may also result in pulmonary edema because of peripheral vascular constriction together with cardiac stimulation. Treatment consists of rapidly acting vasodilators or alpha-adrenergic blocking drugs and/or respiratory support. Epinephrine overdosage can also cause transient bradycardia followed by tachycardia, and these may be accompanied by potentially fatal cardiac arrhythmias. Premature ventricular contractions may appear within one 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. Treatment of arrhythmias consists of administration of a beta-adrenergic blocking drug such as propranolol.

Overdosage sometimes results in extreme pallor and coldness of the skin, metabolic acidosis, and kidney failure. Suitable corrective measures must be taken in such situations.

11 DESCRIPTION

EpiPen® (epinephrine injection, USP) 0.3 mg and EpiPen Jr® (epinephrine injection, USP) 0.15 mg are auto-injectors and combination products containing drug and device components.

Each EpiPen® Auto-Injector, 0.3 mg delivers a single dose of 0.3 mg epinephrine from epinephrine injection, USP 0.3 mg/0.3 mL in a sterile solution. Each EpiPen Jr® Auto-Injector, 0.15 mg delivers a single dose of 0.15 mg epinephrine from epinephrine injection, USP 0.15 mg/0.3 mL in a sterile solution. The EpiPen® and EpiPen Jr® each contain 2 mL epinephrine solution. Approximately 1.7 mL remains in the auto-injector after activation, but is not available for future use, and should be discarded. Each 0.3 mL in the EpiPen® Auto-Injector contains 0.3 mg epinephrine, 1.8 mg sodium chloride, 0.5 mg sodium metabisulfite, hydrochloric acid to adjust pH, and Water for Injection. The pH range is 2.2-5.0. Each 0.3 mL in the EpiPen Jr® Auto-Injector contains 0.15 mg epinephrine, 1.8 mg sodium chloride, 0.5 mg sodium metabisulfite, hydrochloric acid to adjust pH, and Water for Injection. The pH range is 2.2-5.0. Epinephrine is a sympathomimetic catecholamine. Chemically, epinephrine is (-)-3,4-Dihydroxy-α-[(methylamino)methyl]benzyl alcohol with the following structure:



Epinephrine solution deteriorates rapidly on exposure to air or light, turning pink from oxidation to adrenochrome and brown from the formation of melanin. Replace EpiPen® and EpiPen Jr® if the epinephrine solution appears discolored (pinkish or brown color), cloudy, or contains particles.

Thoroughly review the patient instructions and operation of EpiPen® or EpiPen Jr® with patients and caregivers prior to use [see *Patient Counseling Information* (17)].

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Epinephrine acts on both alpha- and beta-adrenergic receptors.

12.2 Pharmacodynamics

Through its action on alpha-adrenergic receptors, epinephrine lessens the vasodilation and increased vascular permeability that occurs during anaphylaxis, which can lead to loss of intravascular fluid volume and hypotension.

Through its action on beta-adrenergic receptors, epinephrine causes bronchial smooth muscle relaxation and helps alleviate bronchospasm, wheezing and dyspnea that may occur during anaphylaxis.

Epinephrine also alleviates pruritus, urticaria, and angioedema and may relieve gastrointestinal and genitourinary symptoms associated with anaphylaxis because of its relaxer effects on the smooth muscle of the stomach, intestine, uterus and urinary bladder.

When given subcutaneously or intramuscularly, epinephrine has a rapid onset and short duration of action.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies to evaluate the carcinogenic potential of epinephrine have not been conducted.

Epinephrine and other catecholamines have been shown to have mutagenic potential *in vitro* and to be an oxidative mutagen in a *WP2* bacterial reverse mutation assay.

Epinephrine was positive in the DNA Repair test with *B. subtilis* (REC) assay, but was not mutagenic in the *Salmonella* bacterial reverse mutation assay.

The potential for epinephrine to impair fertility has not been evaluated.

This should not prevent the use of epinephrine under the conditions noted under *Indications and Usage* (1).

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

EpiPen® Auto-Injectors (epinephrine injections, USP, 0.3 mg/0.3 mL) are available as EpiPen 2-Pak®, NDC 49502-500-02, a pack that contains two EpiPen® Auto-Injectors (epinephrine injections, USP, 0.3 mg/0.3 mL) and one EpiPen® Auto-Injector trainer device. EpiPen Jr® Auto-Injectors (epinephrine injections, USP, 0.15 mg/0.3 mL) are available as EpiPen Jr 2-Pak®, NDC 49502-501-02, a pack that contains two EpiPen Jr® Auto-Injectors (epinephrine injections, USP, 0.3mg/0.3 mL) and one EpiPen® Auto-Injector trainer device.

EpiPen 2-Pak® and EpiPen Jr 2-Pak® also include an S-clip to clip two carrier tubes together. Rx only

16.2 Storage and Handling

Protect from light. Epinephrine is light sensitive and should be stored in the carrier tube provided to protect it from light. Store at 20° to 25°C (68° to 77°F); excursions permitted to 15° to 30°C (59° to 86°F) [See USP Controlled Room Temperature]. Do not refrigerate. Before using, check to make sure the solution in the auto-injector is clear and colorless. Replace the auto-injector if the solution is discolored (pinkish or brown color), cloudy, or contains particles.

17 PATIENT COUNSELING INFORMATION

[See *FDA-Approved Patient Labeling (Patient Information and Instructions for Use)*.]

A healthcare provider should review the patient instructions and operation of EpiPen® and EpiPen Jr® in detail, with the patient or caregiver.

Epinephrine is essential for the treatment of anaphylaxis. Patients who are at risk of or with a history of severe allergic reactions (anaphylaxis) to insect stings or bites, foods, drugs, and other allergens, as well as idiopathic and exercise-induced anaphylaxis, should be carefully instructed about the circumstances under which epinephrine should be used.

Administration and Training

Instruct patients and/or caregivers in the appropriate use of EpiPen® and EpiPen Jr®. EpiPen® should be injected into the middle of the outer thigh (through clothing, if necessary). Each device is a single-use injection. Advise patients to seek immediate medical care in conjunction with administration of EpiPen®.

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* (5.2)].

Complete patient information, including dosage, directions for proper administration and precautions can be found inside each EpiPen® or EpiPen Jr® carton. A printed label on the surface of EpiPen® shows instructions for use and a diagram depicting the injection process.

Instruct patients and/or caregivers to use and practice with the Trainer to familiarize themselves with the use of EpiPen® in an allergic emergency. The Trainer device may be used multiple times. A Trainer is provided in 2-Pak cartons.

Adverse Reactions

Epinephrine may produce symptoms and signs that include an increase in heart rate, the sensation of a more forceful heartbeat, palpitations, sweating, nausea and vomiting, difficulty breathing, pallor, dizziness, weakness or shakiness, headache, apprehension, nervousness, or anxiety. These signs and symptoms usually subside rapidly, especially with rest, quiet and recumbency. Patients with hypertension or hyperthyroidism may develop more severe or persistent effects, and patients with coronary artery disease could experience angina. Patients with diabetes may develop increased blood glucose levels following epinephrine administration. Patients with Parkinson's disease may notice a temporary worsening of symptoms [see *Warnings and Precautions* (5.5)].

Accidental Injection

Advise patients to seek immediate medical care in the case of accidental injection. Since epinephrine is a strong vasoconstrictor when injected into the digits, hands, or feet, treatment should be directed at vasodilatation if there is such an accidental injection to these areas [see *Warnings and Precautions* (5.2)].

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. 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* (5.3)].

Storage and Handling

Instruct patients to inspect the epinephrine solution visually through the clear window of the auto-injector periodically. Replace EpiPen® and EpiPen Jr® if the epinephrine solution appears discolored (pinkish or brown color), cloudy, or contains particles. Epinephrine is light sensitive and should be stored in the carrier tube provided to protect it from light. The carrier tube is not waterproof. Instruct patients that EpiPen® and EpiPen Jr® must be used or properly disposed once the blue safety release is removed or after use [see *Dosage and Handling* (16.2)].

Complete patient information, including dosage, directions for proper administration and precautions can be found inside each EpiPen® Auto-Injector carton.

PATIENT INFORMATION and INSTRUCTIONS FOR USE

EPIPEN[®]

(epinephrine injection, USP) Auto-Injector 0.3 mg
EpiPen[®] = one dose of 0.3 mg epinephrine USP 0.3 mg/0.3 mL

EPIPEN JR[®]

(epinephrine injection, USP) Auto-Injector 0.15 mg
EpiPen Jr.[®] = one dose of 0.15 mg epinephrine USP 0.15 mg/0.3 mL

For allergic emergencies (anaphylaxis)

Patient Information

Read this Patient Information Leaflet carefully before using the EpiPen[®] or EpiPen Jr.[®] Auto-Injector and each time you get a refill. There may be new information. You, your parent, caregiver, or others who may be in a position to administer EpiPen[®] or EpiPen Jr.[®] Auto-Injector, should know how to use it before you have an allergic emergency. This information does not take the place of talking with your healthcare provider about your medical condition or your treatment.

What is the most important information I should know about the EpiPen[®] and EpiPen Jr.[®]?

1. EpiPen[®] and EpiPen Jr.[®] contain epinephrine, a medicine used to treat allergic emergencies (anaphylaxis). Anaphylaxis can be life threatening, can happen within minutes, and can be caused by stinging and biting insects, allergy injections, foods, medicines, exercise, or unknown causes. Symptoms of anaphylaxis may include:

- trouble breathing
- wheezing
- hoarseness (changes in the way your voice sounds)
- hives (raised reddened rash that may itch)
- severe itching
- swelling of your face, lips, mouth, or tongue
- skin rash, redness, or swelling
- fast heartbeat
- weak pulse
- feeling very anxious
- confusion
- stomach pain
- losing control of urine or bowel movements (incontinence)
- diarrhea or stomach cramps
- dizziness, fainting, or “passing out” (unconsciousness)

2. **Always carry your EpiPen[®] or EpiPen Jr.[®] with you because you may not know when anaphylaxis may happen.**

Talk to your healthcare provider if you need additional units to keep at work, school, or other locations. Tell your family members, caregivers, and others where you keep your EpiPen[®] or EpiPen Jr.[®] and how to use it before you need it. You may be unable to speak in an allergic emergency.

3. **When you have an allergic emergency (anaphylaxis)**

- **Use EpiPen[®] or EpiPen Jr.[®] right away.**
- **Get emergency medical help right away.** You may need further medical attention. You may need to use a second EpiPen[®] or EpiPen Jr.[®] if symptoms continue or recur. Only a healthcare provider should give additional doses of epinephrine if you need more than 2 injections for a single anaphylaxis episode.

What are EpiPen[®] and EpiPen Jr.[®]?

- EpiPen[®] and EpiPen Jr.[®] are disposable, prefilled automatic injection devices (auto-injectors) used to treat life-threatening, allergic emergencies including anaphylaxis in people who are at risk for or have a history of serious allergic emergencies. Each device contains a single dose of epinephrine.
- EpiPen[®] and EpiPen Jr.[®] are for immediate self (or caregiver) administration and do not take the place of emergency medical care. You should get emergency help right away after using EpiPen[®] and EpiPen Jr.[®].
- EpiPen[®] and EpiPen Jr.[®] are for people who have been prescribed this medicine by their healthcare provider.
- The EpiPen[®] Auto-Injector (0.3 mg) is for patients who weigh 66 pounds or more (30 kilograms or more).
- The EpiPen Jr.[®] Auto-Injector (0.15 mg) is for patients who weigh about 33 to 66 pounds (15 to 30 kilograms).
- It is not known if EpiPen[®] and EpiPen Jr.[®] are safe and effective in children who weigh less than 33 pounds (15 kilograms).

What should I tell my healthcare provider before using the EpiPen[®] or EpiPen Jr.[®]?

Before you use EpiPen[®] or EpiPen Jr.[®], tell your healthcare provider about all your medical conditions, but especially if you:

- have heart problems or high blood pressure
- have diabetes
- have thyroid problems
- have asthma
- have a history of depression
- have Parkinson’s disease
- have any other medical conditions
- are pregnant or plan to become pregnant. It is not known if epinephrine will harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if epinephrine passes into your breast milk.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Tell your healthcare provider of all known allergies.

Especially tell your healthcare provider if you take certain asthma medicines. EpiPen[®] or EpiPen Jr.[®] and other medicines may affect each other, causing side effects. EpiPen[®] or EpiPen Jr.[®] may affect the way other medicines work, and other medicines may affect how EpiPen[®] or EpiPen Jr.[®] work.

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

Use your EpiPen[®] or EpiPen Jr.[®] for treatment of anaphylaxis as prescribed by your healthcare provider, regardless of your medical conditions or the medicines you take.

How should I use EpiPen[®] and EpiPen Jr.[®]?

- Each EpiPen[®] or EpiPen Jr.[®] Auto-Injector contains only 1 dose of medicine.
- EpiPen[®] or EpiPen Jr.[®] should be injected into the middle of your outer thigh (upper leg). It can be injected through your clothing if needed.
- Read the Instructions for Use at the end of this Patient Information Leaflet about the right way to use EpiPen[®] and EpiPen Jr.[®].
- Your healthcare provider will show you how to safely use the EpiPen[®] or EpiPen Jr.[®] Auto-Injector.
- Use your EpiPen[®] or EpiPen Jr.[®] exactly as your healthcare provider tells you to use it. You may need to use a second EpiPen[®] or EpiPen Jr.[®] if symptoms continue or recur. Only a healthcare provider should give additional doses of epinephrine if you need more than 2 injections for a single anaphylaxis episode.
- **Caution: Never put your thumb, fingers, or hand over the orange tip. Never press or push the orange tip with your thumb, fingers, or hand.** The needle comes out of the orange tip. Accidental injection into finger, hands or feet may cause a loss of blood flow to these areas. **If this happens, go immediately to the nearest emergency room.** Tell the healthcare provider where on your body you received the accidental injection.
- Your EpiPen[®] and EpiPen Jr.[®] Auto-Injector may come packaged with an EpiPen[®] Trainer and separate Trainer Instructions for Use. **The EpiPen[®] Trainer has a grey color. The grey EpiPen[®] Trainer contains no medicine and no needle.** Periodically practice with your EpiPen[®] Trainer before an allergic emergency happens to make sure you are able to safely use the real EpiPen[®] and EpiPen Jr.[®] Auto-Injector in an emergency. Always carry your real EpiPen[®] or EpiPen Jr.[®] Auto-Injector with you in case of an allergic emergency. Additional training resources are available at www.epipen.com.
- Do not drop the carrier tube or auto-injector. If the carrier tube or auto-injector is dropped, check for damage and leakage. Dispose of the auto-injector and carrier tube, and replace if damage or leakage is noticed or suspected.

What are the possible side effects of the EpiPen[®] and EpiPen Jr.[®]?

EpiPen[®] and EpiPen Jr.[®] may cause serious side effects.

• **The EpiPen[®] or EpiPen Jr.[®] should only be injected into the middle of your outer thigh (upper leg). Do not inject the EpiPen[®] or EpiPen Jr.[®] into your:**

- veins
- buttocks
- fingers, toes, hands, or feet

If you accidentally inject EpiPen[®] or EpiPen Jr.[®] into any other part of your body, go to the nearest emergency room right away. Tell the healthcare provider where on your body you received the accidental injection.

• Rarely, 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. If you inject a young child with EpiPen[®] or EpiPen Jr.[®], hold their leg firmly in place 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 certain medical conditions, or take certain medicines, your condition may get worse or you may have longer lasting side effects when you use your EpiPen[®] or EpiPen Jr.[®].** Talk to your healthcare provider about all your medical conditions.

Common side effects of EpiPen[®] and EpiPen Jr.[®] include:

- fast, irregular or “pounding” heartbeat
- sweating
- headache
- weakness
- shakiness
- paleness
- feelings of over excitement, nervousness or anxiety
- dizziness
- nausea or vomiting
- breathing problems

These side effects may go away with rest. **Tell your healthcare provider if you have any side effect that bothers you or that does not go away.**

These are not all the possible side effects of the EpiPen[®] or EpiPen Jr.[®]. For more information, ask your healthcare provider or pharmacist.

Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store EpiPen[®] and EpiPen Jr.[®]?

- Store EpiPen[®] and EpiPen Jr.[®] at room temperature between 68° to 77° F (20° to 25° C).
- Protect from light.
- **Do not** expose to extreme cold or heat. For example, **do not** store in your vehicle’s glove box and **do not** store in the refrigerator or freezer.
- Examine the contents in the clear window of your auto-injector periodically. The solution should be clear. If the solution is discolored (pinkish or brown color) or contains solid particles, replace the unit.
- Always keep your EpiPen[®] or EpiPen Jr.[®] Auto-Injector in the carrier tube to protect it from damage; however, the carrier tube is not waterproof.
- The blue safety release helps to prevent accidental injection. Keep the blue safety release on until you need to use EpiPen[®] or EpiPen Jr.[®].
- Your EpiPen[®] or EpiPen Jr.[®] has an expiration date. Replace it before the expiration date.

Keep EpiPen[®] and EpiPen Jr.[®] and all medicines out of the reach of children.

General information about the safe and effective use of EpiPen[®] and EpiPen Jr.[®]

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information Leaflet. Do not use the EpiPen[®] or EpiPen Jr.[®] for a condition for which it was not prescribed. Do not give your EpiPen[®] or EpiPen Jr.[®] to other people.

This Patient Information Leaflet summarizes the most important information about EpiPen[®] and EpiPen Jr.[®]. If you would like more information, talk to your healthcare provider. You can ask your pharmacist or healthcare provider for information about EpiPen[®] and EpiPen Jr.[®] that is written for health professionals.

For more information and video instructions on the use of EpiPen[®] and EpiPen Jr.[®], go to www.epipen.com or call 1-800-395-3376.

What are the ingredients in EpiPen[®] and EpiPen Jr.[®]?

Active Ingredients: Epinephrine

Inactive Ingredients: sodium chloride, sodium metabisulfite, hydrochloric acid, and water.

Important Information

- **The EpiPen[®] Auto-Injector has a yellow colored label.**
- **The EpiPen Jr.[®] Auto-Injector has a green colored label.**
- **The EpiPen[®] Trainer has a grey color and contains no medicine and no needle.**
- **Your auto-injector is designed to work through clothing.**
- **The blue safety release on the EpiPen[®] and EpiPen Jr.[®] Auto-Injector helps to prevent accidental injection of the device. Do not remove the blue safety release until you are ready to use it.**
- **Only inject into the middle of the outer thigh (upper leg). Never inject into any other part of the body.**
- **Never put your thumb, fingers, or your hand over the orange tip. The needle comes out of the orange tip.**
- **If an accidental injection happens, get medical help right away.**
- **Do not place patient information or any other foreign objects in the carrier tube with the Auto-Injector, as this may prevent you from removing the Auto-Injector for use.**

INSTRUCTIONS FOR USE

EPIPEN[®]

(epinephrine injection, USP) Auto-Injector 0.3 mg
EpiPen[®] = one dose of 0.3 mg epinephrine USP 0.3 mg/0.3 mL

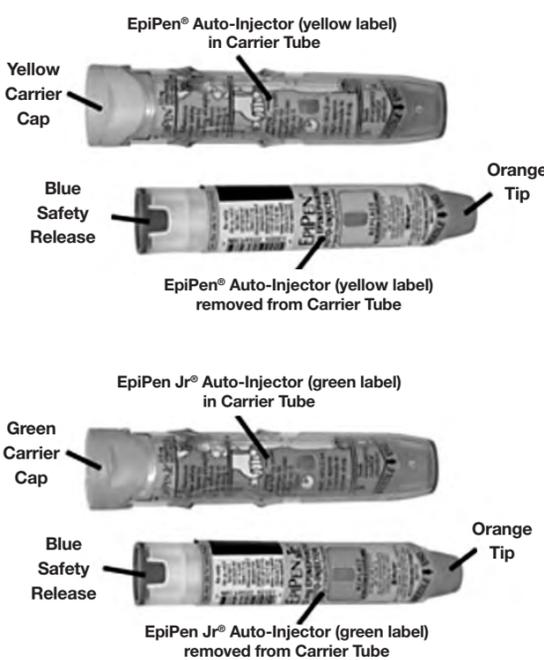
EPIPEN JR[®]

(epinephrine injection, USP) Auto-Injector 0.15 mg
EpiPen Jr.[®] = one dose of 0.15 mg epinephrine USP 0.15 mg/0.3 mL

For allergic emergencies (anaphylaxis)

Read these Instructions for Use carefully before you use EpiPen[®] or EpiPen Jr.[®]. Before you need to use your EpiPen[®] or EpiPen Jr.[®], make sure your healthcare provider shows you the right way to use it. Parents, caregivers, and others who may be in a position to administer EpiPen[®] or EpiPen Jr.[®] Auto-Injector should also understand how to use it as well. If you have any questions, ask your healthcare provider.

Your EpiPen[®] and EpiPen Jr.[®] Auto-Injector



A dose of EpiPen[®] or EpiPen Jr.[®] requires 3 simple steps: Prepare, Administer and Get emergency medical help

Step 1. Prepare EpiPen[®] or EpiPen Jr.[®] for injection



Remove the EpiPen[®] or EpiPen Jr.[®] from the clear carrier tube.

Flip open the yellow cap of your EpiPen[®] or the green cap of your EpiPen Jr.[®] carrier tube.



Tip and slide the auto-injector out of the carrier tube.



Grasp the auto-injector in your fist with the orange tip (needle end) pointing downward.

With your other hand, **remove the blue safety release by pulling straight up** without bending or twisting it.

Note:

- The needle comes out of the orange tip.
- To avoid an accidental injection, never put your thumb, fingers or hand over the orange tip. If an accidental injection happens, get medical help right away

Step 2. Administer EpiPen[®] or EpiPen Jr.[®]

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



Place the orange tip against the middle of the outer thigh (upper leg) at a right angle (perpendicular) 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).

The injection is now complete.



Remove the auto-injector from the thigh.

The orange tip will extend to cover the needle. If the needle is still visible, do not attempt to reuse it.



Massage the injection area for 10 seconds.

Step 3. Get emergency medical help now.

You may need further medical attention. **You may need to use a second EpiPen[®] or EpiPen Jr.[®] Auto-Injector if symptoms continue or recur.**

- Take your used auto-injector with you when you go to see a healthcare provider.
- Tell the healthcare provider that you have received an injection of epinephrine. Show the healthcare provider where you received the injection.
- Give your used EpiPen[®] or EpiPen Jr.[®] Auto-Injector to the healthcare provider for inspection and proper disposal.
- Ask for a refill, if needed.

Note:

- The used auto-injector with extended needle cover will not fit in the carrier tube.
- EpiPen[®] and EpiPen Jr.[®] are single-use injectable devices that deliver a fixed dose of epinephrine. The auto-injector cannot be reused. Do not attempt to reuse EpiPen[®] after the device has been activated. It is normal for most of the medicine to remain in the auto-injector after the dose is injected. The correct dose has been administered if the orange needle tip is extended and the window is blocked.
- Your EpiPen[®] and EpiPen Jr.[®] Auto-Injector may come packaged with an EpiPen[®] Trainer and separate Trainer Instructions for Use. The EpiPen[®] Trainer has a grey color. The grey EpiPen[®] Trainer contains no medicine and no needle. Practice with your EpiPen[®] Trainer, but always carry your real EpiPen[®] or EpiPen Jr.[®] Auto-Injector in case of an allergic emergency.
- If you will be administering EpiPen[®] or EpiPen Jr.[®] to a young child, ask your healthcare provider to show you how to properly hold the leg in place while administering a dose.
- Do not try to take the EpiPen[®] or EpiPen Jr.[®] Auto-Injector apart.

This Patient Information and Instructions for Use has been approved by the U.S. Food and Drug Administration.

Manufactured for Mylan Specialty L.P., Morgantown, WV 26505, U.S.A. by Meridian Medical Technologies, Inc., Columbia, MD 21046, U.S.A., a Pfizer company.

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(epinephrine injection, USP) Auto-Injector 0.15 mg
EpiPen Jr.[®] = one dose of 0.15 mg epinephrine USP 0.15 mg/0.3 mL

MyEpiPen.com

Register your EpiPen[®] or EpiPen Jr.[®] Auto-Injector at MyEpiPen.com and find out more about:

- Free EpiPen[®] Auto-Injector **Refill Reminder Program**. It is important to keep your auto-injector up-to-date.

Register up to 6 EpiPen[®] or EpiPen Jr.[®] Auto-Injectors and receive automatic **Refill Reminder Alerts**.

- Receive periodic information related to allergies and allergens.
- Instructional Video

For more information about EpiPen[®] or EpiPen Jr.[®] Auto-Injectors and proper use of the product, call Mylan at 1-877-446-3679 or visit www.epipen.com.