Considerations for the Pharmacist About Anaphylaxis and Epinephrine Auto-Injectors

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KEY TAKEAWAYS

- *Anaphylaxis is an acute, severe, and potentially life-threatening systemic allergic reaction.*[1]
- *Epinephrine is the first-line treatment for anaphylaxis.*[2]
- *Antihistamines are commonly used in the treatment of anaphylaxis; however, the use of antihistamines alone may increase the risk of progression toward a life-threatening reaction.*[2]
- *Patients at risk for anaphylaxis should have 2 doses of epinephrine available at all times.*[2]

Anaphylaxis is an acute, severe, potentially life-threatening systemic allergic reaction caused by the sudden release of mast cell and basophil mediators.[1] Triggers for anaphylactic reactions may include foods (eg, peanuts, tree nuts, fish, shellfish, cow's milk, soy, eggs), natural rubber latex, medications (eg, general anesthesia, penicillin), and insect stings.[1,3] The onset of the anaphylactic reaction generally occurs within seconds or minutes of exposure to the injected or ingested allergen, although the timing of the emergence of signs and symptoms varies from person to person. Generally, the signs and symptoms of anaphylaxis affect the skin and the respiratory, circulatory, and gastrointestinal systems; the most serious symptoms are low blood pressure, difficulty breathing, and loss of consciousness (Table).[1,3,4] An anaphylactic reaction can involve upper or lower airway obstruction or both; patients may have laryngeal edema that they describe as a "lump" in the throat, or a bronchial obstruction that may manifest as wheezing or a feeling of tightness in the chest. A characteristic skin feature is the appearance of well-circumscribed cutaneous wheals that are intensely pruritic and can be disseminated or localized.[3] The overall incidence of anaphylaxis is estimated to be between 1% and 2%.[5] Of note, up to 20% of patients with anaphylaxis will experience a 2-phase reaction—an initial reaction followed by a second reaction.[6] The reported time to onset of the second reaction ranges from 1 to 78 hours; however, most occur within 8 hours.[7] Protracted severe anaphylaxis can last up to 32 hours despite treatment.[1]

As anaphylaxis is potentially fatal, immediate symptom recognition and treatment are required.[3] According to

TABLE: FREQUENCY OF OCCURRENCE OF SIGNS AND SYMPTOMS OF ANAPHYLAXIS[1,a-c]

Signs and Symptoms	Percent
Cutaneous	
Urticaria and angioedema	85-90
Flushing	45-55
Pruritus without rash	2-5
Respiratory	
Dyspnea, wheeze	45-50
Upper airway angioedema	50-60
Rhinitis	15-20
Dizziness, syncope, hypotension	30-35
Abdominal	
Nausea, vomiting, diarrhea, cramping pain	25-30
Miscellaneous	
Headache	5-8
Substernal pain	4-6
Seizure	1-2

[a]Based on a compilation of 1865 patients.
[b]Percentages are approximations.
[c]Children may have a lower frequency of cutaneous symptoms in anaphylaxis.

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joint guidelines from the American Academy of Allergy, Asthma & Immunology; the American College of Allergy, Asthma & Immunology; and the Joint Council of Allergy, Asthma and Immunology, injectable epinephrine is the treatment of choice.[1] Guidelines from the National Institute of Allergy and Infectious Diseases (NIAID) also recommend the use of injectable epinephrine as first-line treatment for anaphylaxis. If there is a suboptimal response to epinephrine or if symptoms progress, a repeat dose of epinephrine is recommended over the use of other therapies. Antihistamines are commonly used in the treatment of anaphylaxis; however, the use of antihistamines alone may increase the risk of progression toward a life-threatening reaction.[2] All patients who have had anaphylactic reactions should be counseled on allergen avoidance measures.[1] NIAID guidelines recommend that patients carry 2 doses of epinephrine with them at all times.[2]

About EpiPen Auto-Injector

EpiPen (epinephrine) Auto-Injector and EpiPen Jr Auto-Injector are indicated in the emergency treatment of allergic reactions (type I) including anaphylaxis to stinging insects (eg, order Hymenoptera, which includes bees, wasps, hornets, yellow jackets, and fire ants) and biting insects (eg, triatoma, mosquitos), allergen immunotherapy, foods, drugs, diagnostic testing substances (eg, radiocontrast media), and other allergens, as well as idiopathic anaphylaxis or exercise-induced anaphylaxis.[8]

There are no absolute contraindications to the use of epinephrine in a life-threatening situation. Adverse reactions include transient, moderate anxiety; apprehensiveness; restlessness; tremor; weakness; dizziness; sweating; palpitations; pallor; nausea and vomiting; headache; and/or respiratory difficulties. Arrhythmias, including fatal ventricular fibrillation, have been reported in patients with underlying cardiac disease or who are taking certain drugs (ie, cardiac glycosides or diuretics). Rapid rises in blood pressure have produced cerebral hemorrhage, particularly in elderly patients with cardiovascular disease. Angina may occur in patients with coronary artery disease.[8]

The EpiPen Auto-Injector is supplied as a 2-pak carton (ie, 2 auto-injectors) that also includes 1 training device and is available in 2 different doses, 0.3 mg or 0.15 mg. The 0.3-mg dose is intended for patients who weigh 66 pounds or more, whereas the 0.15-mg dose is intended for patients who weigh between 33 and 66 pounds.[8]

According to the FDA Therapeutic Equivalence Evaluation Code (Orange Book), EpiPen Auto-Injector and EpiPen Jr Auto-Injector have been assigned a BX equivalence code and are not therapeutically equivalent to other epinephrine auto-injector products. The BX code is assigned when there are known or potential bioequivalence problems or when there are insufficient data to support bioequivalence. By contrast, the AB code is assigned when bioequivalence requirements have been met; AB-rated products are considered therapeutically equivalent to other products.[9] Although generic substitution laws vary by state, many states allow generic substitution based on therapeutic equivalency (AB rating) as listed in the Orange Book. Pharmacists who dispense epinephrine to patients with a history of anaphylaxis should be aware that there are no AB-rated generic equivalents to EpiPen Auto-Injector and EpiPen Jr Auto-Injector.[10]

Role of the Pharmacist

EpiPen Auto-Injector was approved by the FDA in 1987 and has a long history of use.[9] Other epinephrine auto-

Please see additional Important Safety Information on next page and full Prescribing Information on the following pages.

Indications

EpiPen® (epinephrine) 0.3 mg and EpiPen Jr® (epinephrine) 0.15 mg Auto-Injectors are indicated in the emergency treatment of type 1 allergic reactions, including anaphylaxis, to allergens, idiopathic and exercise-induced anaphylaxis, and in patients with a history or increased risk of anaphylactic reactions. Selection of the appropriate dosage strength is determined according to body weight.

Important Safety Information

EpiPen Auto-Injectors should only be injected into the anterolateral aspect of the thigh. DO NOT INJECT INTO BUTTOCK, OR INTRAVENOUSLY.

Epinephrine should be used with caution in patients with certain heart diseases, and in patients who are on drugs that may sensitize the heart to arrhythmias, because it may precipitate or aggravate angina pectoris and produce ventricular arrhythmias. Arrhythmias, including fatal ventricular fibrillation, have been reported in patients with underlying cardiac disease or taking cardiac glycosides or diuretics. Patients with certain medical conditions or who take certain medications for allergies, depression, thyroid disorders, diabetes, and hyperten-

injector products use the same drug and dosage but a different delivery device.[11-13] It is important to note that patients will often have received training on a particular prescribed epinephrine device; therefore, if a different device is dispensed, additional training may be warranted.

Patients may present to the pharmacy with a prescription for multiple 2-pak cartons so that they have 2 doses of epinephrine available in several locations (eg, home, car, office). Up to 20% of patients with anaphylaxis will experience a 2-phase reaction, and a second dose of epinephrine may be needed if symptoms progress or if there is a suboptimal response to epinephrine.[2,6] Pharmacists should consider keeping sufficient stock on hand to accommodate the dispensing of multiple 2-pak cartons. It also may be necessary at times to dispense one 2-pak carton with the remainder of prescription dispensed another day. Pharmacists should let patients know when they can come back for the remainder of the prescription, and remind patients of the importance of coming back so that they have multiple 2-pak cartons to keep in locations where they may be needed. When processing the pharmacy claim, it is important to note that Medi-Span has designated the EpiPen Auto-Injector 2-pak carton as a 1-day supply.[14]

Counseling topics for patients with anaphylaxis include avoiding known allergens and recognizing the symptoms of a life-threatening allergic reaction. Patients should also be informed about the potential for a 2-phase reaction that could result in a need for multiple epinephrine injections. Patients should receive training on the use of the epinephrine auto-injector and should also strongly consider training family and friends on the use of the auto-injector, in the event that assistance is needed. Patients should also be advised that using an auto-injector is not a substitute for emergency medical attention. Following usage of the auto-injector, patients should make a follow-up appointment with their allergist/immunologist.[1] Other counseling points should include storing epinephrine auto-injectors properly and keeping epinephrine auto-injectors on hand wherever they may be needed (eg, home, car, office). Importantly, patients should be instructed to regularly check the expiration date on all epinephrine auto-injectors. By counseling patients on avoidance of known allergens, proper device usage, prompt symptom recognition, and appropriate device storage, pharmacists can help improve outcomes during emergency medical situations involving anaphylaxis.

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PRESCRIBING INFORMATION

EPIPEN®

(epinephrine) Auto-Injector 0.3 mg

EpiPen® = one dose of 0.30 mg epinephrine (USP, 1:1000, 0.3 mL)

EPIPEN JR®

(epinephrine) Auto-Injector 0.15 mg

EpiPen Jr® = one dose of 0.15 mg epinephrine (USP, 1:2000, 0.3 mL)

DESCRIPTION

Each EpiPen® Auto-Injector delivers **a single dose** of 0.3 mg epinephrine injection, USP, 1:1000 (0.3 mL) in a sterile solution.

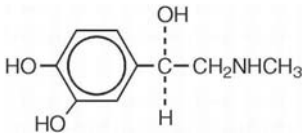
Each EpiPen Jr® Auto-Injector delivers **a single dose** of 0.15 mg epinephrine injection, USP, 1:2000 (0.3 mL) in a sterile solution.

The EpiPen Auto-Injector and EpiPen Jr Auto-Injector (henceforth referred to as EpiPen and EpiPen Jr Auto-Injector) each contain 2 mL epinephrine solution. Approximately 1.7 mL remains in the auto-injector after activation and cannot be used.

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 B-(3, 4-dihydroxyphenyl)-a-methyl-aminoethanol, 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 Auto-Injectors if the epinephrine solution appears discolored.

EpiPen and EpiPen Jr Auto-Injectors do not contain latex.

CLINICAL PHARMACOLOGY

Epinephrine is the drug of choice for the emergency treatment of severe allergic reactions (Type I) to insect stings or bites, foods, drugs, and other allergens. It can also be used in the treatment of anaphylaxis of unknown cause (idiopathic anaphylaxis) or exercise-induced anaphylaxis. When given intramuscularly or subcutaneously it has a rapid onset and short duration of action. Epinephrine acts on both alpha and beta adrenergic receptors. 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 that helps alleviate bronchospasm, wheezing and dyspnea that may occur during anaphylaxis. Epinephrine also alleviates pruritus, urticaria, and angioedema and may be effective in relieving gastrointestinal and genitourinary symptoms associated with anaphylaxis because of its relaxer effects on the smooth muscle of the stomach, intestine, uterus, and urinary bladder.

INDICATIONS AND USAGE

EpiPen and EpiPen Jr Auto-Injectors 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, mosquitos), 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 Auto-Injectors 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. Selection of the appropriate dosage strength is determined according to patient body weight (see **DOSAGE AND ADMINISTRATION** section).

Such 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 Auto-Injectors are intended for immediate self-administration as emergency supportive therapy only and are not a substitute for immediate medical care.

CONTRAINDICATIONS

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

WARNINGS

EpiPen and EpiPen Jr Auto-Injectors should **only** be injected into the anterolateral aspect of the thigh. 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.

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. Treatment should be directed at vasodilation in addition to further treatment of anaphylaxis (see **ADVERSE REACTIONS**). 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.

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.

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. 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 should be administered with caution in 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, e.g., digitalis, diuretics, or anti-arrhythmics, epinephrine may precipitate or aggravate angina pectoris as well as produce ventricular arrhythmias. It should be recognized that the presence of these conditions is not a contraindication to epinephrine administration in an acute, life-threatening situation.

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

PRECAUTIONS

(1) General

EpiPen and EpiPen Jr Auto-Injectors 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.

Epinephrine is essential for the treatment of anaphylaxis. Patients 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. It must be clearly determined that the patient is at risk of future anaphylaxis, since the following risks may be associated with epinephrine administration (see **DOSAGE and ADMINISTRATION**).

Epinephrine should be used with caution in patients who have cardiac arrhythmias, coronary artery or organic heart disease, hypertension, or in patients who are on drugs that may sensitize the heart to arrhythmias, e.g., digitalis, diuretics, quinidine, or other anti-arrhythmics. In such patients, epinephrine may precipitate or aggravate angina pectoris as well as produce ventricular arrhythmias.

The effects of epinephrine may be potentiated by tricyclic antidepressants and monoamine oxidase inhibitors.

Some patients may be at greater risk of developing adverse reactions after epinephrine administration. These include: hyperthyroid individuals, individuals with cardiovascular disease, hypertension, or diabetes, elderly individuals, pregnant women, pediatric patients under 30 kg (66 lbs.) body weight using EpiPen Auto-Injector, and pediatric patients under 15 kg (33 lbs.) body weight using EpiPen Jr Auto-Injector.

Despite these concerns, epinephrine is essential for the treatment of anaphylaxis. Therefore, patients with these conditions, and/or any other person who might be in a position to administer EpiPen or EpiPen Jr Auto-Injector to a patient experiencing anaphylaxis should be carefully instructed in regard to the circumstances under which epinephrine should be used.

(2) Information for Patients

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

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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 symptoms and signs 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.

In case of accidental injection, the patient should be advised to immediately go to the emergency room for treatment. Since the epinephrine in the EpiPen Auto-Injector is a strong vasoconstrictor when injected into the digits, hands or feet, treatment should be directed at vasodilation if there is such an inadvertent administration to these areas (see **ADVERSE REACTIONS**).

The carrier tube is not waterproof.

The blue safety release helps prevent accidental injection and should be kept on until it will be used.

(3) Drug Interactions

Patients who receive epinephrine while concomitantly taking cardiac glycosides or diuretics should be observed carefully for the development of cardiac arrhythmias.

The effects of epinephrine may be potentiated by tricyclic antidepressants, monoamine oxidase inhibitors, levothyroxine sodium, and certain antihistamines, notably chlorpheniramine, tripelennamine 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 phentoloamine. Ergot alkaloids may also reverse the pressor effects of epinephrine.

(4) Carcinogenesis, Mutagenesis, Impairment of Fertility

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 had a moderate degree of mutagenicity, and was positive in the DNA Repair test with *B. subtilis* (REC) assay, but was not mutagenic in the *Salmonella* bacterial reverse mutation assay.

Studies of epinephrine after repeated exposure in animals to evaluate the carcinogenic and mutagenic potential or the effect on fertility have not been conducted. This should not prevent the use of epinephrine under the conditions noted under **INDICATIONS AND USAGE**.

(5) Usage in Pregnancy

Pregnancy Category C: There is no study on the acute effect of epinephrine on pregnancy. Epinephrine has been shown to have developmental effects when administered subcutaneously in rabbits at a dose of 1.2 mg/kg daily for two to three days (approximately 30 times the maximum recommended daily subcutaneous or intramuscular dose on a mg/m^2 basis), in mice at a subcutaneous dose of 1 mg/kg daily for 10 days (approximately 7 times the maximum daily subcutaneous or intramuscular dose on a mg/m^2 basis) and in hamsters at a subcutaneous dose of 0.5 mg/kg daily for 4 days (approximately 5 times the maximum recommended daily subcutaneous or intramuscular dose on a mg/m^2 basis). These effects were not seen in mice at a subcutaneous dose of 0.5 mg/kg daily for 10 days (approximately 3 times the maximum recommended daily subcutaneous or intramuscular dose on a mg/m^2 basis). 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.

It is not known if epinephrine passes into breast milk.

ADVERSE REACTIONS

Adverse reactions to epinephrine include transient, moderate 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. Arrhythmias, including fatal ventricular fibrillation, have been reported in patients with underlying cardiac disease or certain drugs (see **PRECAUTIONS, Drug Interactions**). Rapid rises in blood pressure have produced cerebral hemorrhage, particularly in elderly patients with cardiovascular disease. Angina may occur in patients with coronary artery disease. The potential for epinephrine to produce these types of adverse reactions does not contraindicate its use in an acute life-threatening allergic reaction.

Accidental injection into the digits, hands or feet may result in loss of blood flow to the affected area (see **WARNINGS**). Adverse events experienced as a result of accidental injections may include increased heart rate, local reactions including injection site pallor, coldness and hypoaesthesia or injury at the injection site resulting in bruising, bleeding, discoloration, erythema or skeletal injury.

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 may also result in pulmonary edema because of peripheral vascular constriction together with cardiac stimulation. Treatment consists of a rapidly acting alpha-adrenergic blocking drug 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-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.

DOSAGE AND ADMINISTRATION

EpiPen or EpiPen Jr Auto-Injector prescribers should ensure that the patient or caregiver understands the indications and use of this product. A healthcare provider should review the patient instructions and operation of the EpiPen or EpiPen Jr Auto-Injector, in detail, with the patient or caregiver. Inject EpiPen or EpiPen Jr intramuscularly or subcutaneously into the anterolateral aspect of the thigh, through clothing if necessary. See detailed Directions for Use on the accompanying Patient Instructions.

Selection of the appropriate dosage strength is determined according to patient body weight.

EpiPen Auto-Injector delivers 0.3 mg epinephrine injection (0.3 mL, 1:1000) and is intended for patients who weigh 30 kg or more (approximately 66 pounds or more).

EpiPen Jr Auto-Injector delivers 0.15 mg epinephrine injection (0.3 mL, 1:2000) and is intended for patients who weigh 15 to 30 kg (33 – 66 pounds).

Each EpiPen or EpiPen Jr Auto-Injector contains a single dose of epinephrine. Since the doses of epinephrine delivered from EpiPen or EpiPen Jr Auto-Injector 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 Auto-Injector may be necessary.

Patients should be instructed to periodically visually inspect the epinephrine solution for particulate matter and discoloration. If the solution contains particulate matter or develops a pinkish or brown color, the patient should immediately contact their physician for a replacement, since these changes indicate that the effectiveness of the drug product may be decreased.

HOW SUPPLIED

EpiPen Auto-Injectors (epinephrine injections, USP, 1:1000, 0.3 mL) are available in individual cartons, NDC 49502-500-01, and as EpiPen 2-Pak®, NDC 49502-500-02, a pack that contains two EpiPen Auto-Injectors (epinephrine injections, USP, 1:1000, 0.3 mL) and one EpiPen Auto-Injector trainer device.

EpiPen Jr Auto-Injectors (epinephrine injection, USP, 1:2000, 0.3 mL) are available in individual cartons, NDC 49502-501-01, and as EpiPen Jr 2-Pak®, NDC 49502-501-02, a pack that contains two EpiPen Jr Auto-Injectors (epinephrine injections, USP, 1:2000, 0.3 mL) and one EpiPen Auto-Injector trainer device.

EpiPen 2-Pak® and EpiPen Jr 2-Pak® also includes an S-clip to clip two cases together.

Store at 20° to 25°C (68° to 77°F); excursions permitted to 15°C-30°C (59°F-86°F) (See USP Controlled Room Temperature). Do not refrigerate. Protect from light. Contains no latex.

Rx only.

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