

HIGHLIGHTS OF PRESCRIBING INFORMATION

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

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

INDICATIONS AND USAGE

Adrenaclick contains 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): Adrenaclick 0.3 mg (2)
- Patients 15 to 30 kg (33 lbs-66 lbs): Adrenaclick 0.15 mg (2)

Inject Adrenaclick 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

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

- The presence of a sulfite in this product should not deter use. (5.3)
- Administer with caution in patients with heart disease; may aggravate angina pectoris or produce ventricular arrhythmias. (5.4)

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 Amedra Pharmaceuticals LLC at 1-888-894-6528 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. (5.4, 8.5)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 10/2014

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Adrenaclick[®] is indicated in the emergency treatment of allergic reactions (Type I) including anaphylaxis to stinging insects (e.g., order Hymenoptera, which includes 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.

Adrenaclick is 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.

Adrenaclick is intended for immediate administration as emergency supportive therapy only and is not a replacement or substitute for immediate medical care.

2 DOSAGE AND ADMINISTRATION

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

- Patients greater than or equal to 30 kg (approximately 66 pounds or more): Adrenaclick 0.3 mg
- Patients 15 to 30 kg (33 pounds to 66 pounds): Adrenaclick 0.15 mg

Inject Adrenaclick intramuscularly or subcutaneously into the anterolateral aspect of the thigh, through clothing if necessary.

Each Adrenaclick contains a single dose of epinephrine for single use injection. Since the doses of epinephrine delivered from Adrenaclick 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 Adrenaclick 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 viewing window of Adrenaclick should be inspected visually for particulate matter and discoloration. Epinephrine is light sensitive and should be stored in the outer case provided to protect it from light [*see How Supplied/Storage and Handling (16.2)*].

3 **DOSAGE FORMS AND STRENGTHS**

- Injection, 0.3 mg/0.3 mL epinephrine injection, USP, pre-filled auto-injector
- Injection, 0.15 mg/0.15 mL epinephrine injection, USP, pre-filled auto-injector

4 **CONTRAINDICATIONS**

None.

5 **WARNINGS AND PRECAUTIONS**

5.1 **Emergency Treatment**

Adrenacllick is intended for immediate administration as emergency supportive therapy and is 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 **Incorrect Locations of Injection**

Adrenacllick 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 a 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 the development of gas gangrene. Cleansing with alcohol does not kill bacterial spores, and therefore, does not lower the 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)*].

5.3 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 bisulfite, 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.

5.4 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 Adrenaclick 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 (5.4)*].

Arrhythmias, including fatal ventricular fibrillation, have been reported, particularly in patients with underlying cardiac disease or those receiving certain drugs [*see Warnings and Precautions (5.4) and Drug Interactions (7)*].

Rapid rises in blood pressure have produced cerebral hemorrhage, particularly in elderly patients with cardiovascular disease [*see Warnings and Precautions (5.4)*].

Angina may occur in patients with coronary artery disease [*see Warnings and Precautions (5.4)*].

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.

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

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 (5.4)*].

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 Adrenacllick is administered to a nursing woman.

8.4 Pediatric Use

Adrenacllick 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 dose of epinephrine delivered from Adrenacllick is 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, Adrenacllick 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 (5.4) and 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 a 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

Adrenacllick (epinephrine injection, USP) auto-injector 0.3 mg and 0.15 mg is an auto-injector and a combination product containing drug and device components.

Each Adrenacllick 0.3 mg delivers a single dose of 0.3 mg epinephrine from epinephrine injection, USP (0.3 mL) in a sterile solution.

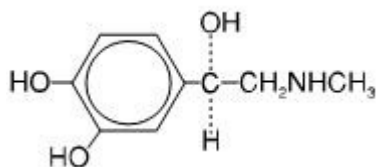
Each Adrenacllick 0.15 mg delivers a single dose of 0.15 mg epinephrine from epinephrine injection, USP (0.15 mL) in a sterile solution.

Adrenacllick 0.3 mg and Adrenacllick 0.15 mg each contain 1.1 mL of epinephrine solution. 0.3 mL and 0.15 mL epinephrine solution are dispensed for Adrenacllick 0.3 mg and Adrenacllick 0.15 mg, respectively, when activated. The solution remaining after activation is not available for future use and should be discarded.

Each 0.3 mL in Adrenacllick 0.3 mg contains 0.3 mg epinephrine, 2.6 mg sodium chloride, not more than 1.5 mg chlorobutanol, 0.45 mg sodium bisulfite, hydrochloric acid and sodium hydroxide to adjust pH, and water for injection. The pH range is 2.2-5.0.

Each 0.15 mL in Adrenacllick 0.15 mg contains 0.15 mg epinephrine, 1.3 mg sodium chloride, not more than 0.75 mg chlorobutanol, 0.225 sodium bisulfite, hydrochloric acid and sodium hydroxide 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 Adrenacllick if the epinephrine solution appears discolored (pinkish or brown color), cloudy, or contains particles.

Thoroughly review the patient instructions and operation of Adrenacllick 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 intramuscularly or subcutaneously, 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

Carton containing two AdrenaClick (epinephrine injection, USP) 0.3 mg auto-injectors:
NDC 52054-804-02.

Carton containing two AdrenaClick (epinephrine injection, USP) 0.15 mg auto-injectors:
NDC 52054-803-02.

Rx only

16.2 Storage and Handling

Protect from light. Epinephrine is light sensitive and should be stored in the carrying-case provided to protect it from light. Store at room temperature (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 Adrenaclick, 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

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

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

Patients and/or caregivers should be instructed to use the Trainer to familiarize themselves with the use of Adrenaclick in an allergic emergency. The Trainer may be used multiple times.

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 (5.4)*].

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 vasodilation if there is such an accidental injection to these areas [see *Warnings and Precautions (5.2)*].

Storage and Handling

Instruct patients to inspect the epinephrine solution visually through the viewing window periodically. Adrenaclick should be replaced if the epinephrine solution appears discolored (pinkish or brown), cloudy, or contains particles. Epinephrine is light sensitive and should be stored in the outer case provided to protect it from light. Patients should be instructed that Adrenaclick must be properly disposed of once the blue caps have been removed or after use [*see How Supplied/Storage and Handling (16.2)*].

Complete patient information, including dosage, directions for proper administration and precautions are provided inside each Adrenaclick auto-injector carton.

Manufactured for and Distributed by: Amedra Pharmaceuticals LLC, Horsham, PA 19044

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For inquiries call 1-888-894-6528

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Patient Information

ADRENACLICK® (a-dren-a-click)

(epinephrine injection)

auto-injector

For allergic emergencies (anaphylaxis)

Read this Patient Information Leaflet carefully before you use the Adrenaclick 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 Adrenaclick 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 Adrenaclick?

1. Adrenaclick contains 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 other unknown causes. Symptoms of an 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 Adrenaclick 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 Adrenaclick 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 Adrenaclick right away.**
 - **Get emergency medical help right away.** You may need further medical attention. You may need to use a second Adrenaclick auto-injector 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 is Adrenaclick?

- Adrenaclick is a disposable, prefilled automatic injection device (auto-injector) 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.
- Adrenaclick is for immediate self (or caregiver) administration and does not take the place of emergency medical care. You should get emergency medical help right away after using Adrenaclick.
- Adrenaclick is for people who have been prescribed this medicine by their healthcare provider.
- The Adrenaclick 0.3 mg auto-injector is for patients who weigh 66 pounds or more (30 kilograms or more).
- The Adrenaclick 0.15 mg auto-injector is for patients who weigh about 33 to 66 pounds (15 to 30 kilograms).
- It is not known if Adrenaclick is safe and effective in children who weigh less than 33 pounds (15 kilograms).

What should I tell my healthcare provider before using Adrenaclick?

Before you use Adrenaclick, tell your healthcare provider about all your medical conditions, 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.

Adrenaclick and other medicines may affect each other, causing side effects. Adrenaclick may affect the way other medicines work, and other medicines may affect how Adrenaclick works.

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 Adrenaclick auto-injector for treatment of anaphylaxis as prescribed by your healthcare provider, regardless of your medical conditions or the medicine you take.

How should I use Adrenaclick?

- Each Adrenaclick auto-injector contains only 1 dose of medicine.
- Adrenaclick should only be injected into the middle of the outer thigh (upper leg). It can be injected through clothing, if needed.
- Read the Instructions for Use at the end of this Patient Information Leaflet for information about the right way to use Adrenaclick.
- Your healthcare provider will show you how to safely use the Adrenaclick auto-injector.
- Use Adrenaclick exactly as your healthcare provider tells you to use it. You may need to use a second Adrenaclick auto-injector 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 red tip. Never press or push the red tip with your thumb, fingers, or hand.** The needle comes out of the red tip. Accidental injection into finger, hands, or feet may cause a loss of blood flow to those 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 Adrenaclick auto-injector comes packaged in a carton containing 2 Adrenaclick auto-injectors.

- You may request a separate Trainer, that comes packaged with Trainer Instructions for Use. Additional video instructions on the use of Adrenaclick are available from www.adrenaclick.com. **The Adrenaclick Trainer has a beige color. The beige Adrenaclick Trainer contains no medicine and no needle.** Practice with your Adrenaclick Trainer before an allergic emergency happens to make sure you are able to safely use the real Adrenaclick auto-injector in an emergency. Always carry your real Adrenaclick auto-injector with you in case of an allergic emergency.
- Do not drop the carrying case or Adrenaclick auto-injector. If the carrying case or Adrenaclick auto-injector is dropped, check for damage and leakage. Dispose of the auto-injector and carrying case, and replace if damage or leakage is noticed or suspected.

What are the possible side effects of Adrenaclick?

Adrenaclick may cause serious side effects.

- **Adrenaclick should only be injected into the middle of your outer thigh (upper leg). Do not** inject Adrenaclick into your:
 - veins
 - buttocks
 - fingers, toes, hands or feet.

If you accidentally inject Adrenaclick 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.

- **If you have certain medical conditions, or take certain medicines, your condition may get worse or you may have more or longer lasting side effects when you use Adrenaclick.** Talk to your healthcare provider about all your medical conditions.

Common side effects of Adrenaclick include:

- faster, 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 Adrenaclick. 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 Adrenaclick?

- Store Adrenaclick at room temperature between 68° to 77° F (20° to 25° C).
- Protect from light.
- **Do not** expose to extreme heat or cold. 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 viewing window of your auto-injector periodically. The solution should be clear. If the solution is discolored (pinkish or brown), cloudy or contains solid particles, replace the unit.
- Always keep your Adrenaclick auto-injector in the carrying case to protect it from damage; however, the carrying case is not waterproof.
- The two blue end caps help to prevent accidental injection. Do not remove the blue end caps until you are ready to use Adrenaclick.
- Your Adrenaclick has an expiration date. Replace it before the expiration date.

Keep Adrenaclick and all medicines out of the reach of children.

General information about the safe and effective use of Adrenaclick:

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information Leaflet. Do not use Adrenaclick for a condition for which it was not prescribed. Do not give Adrenaclick to other people.

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

For more information and video instructions on the use of Adrenaclick, go to www.adrenaclick.com or call 1-888-894-6528.

What are the ingredients in Adrenaclick?

Active Ingredient: epinephrine

Inactive Ingredients: sodium chloride, chlorobutanol, sodium bisulfite, hydrochloric acid and sodium hydroxide, and water.

Important Information

- The Adrenaclick 0.3 mg auto-injector has a yellow colored label.
- The Adrenaclick 0.15 mg auto-injector has an orange colored label.
- The Adrenaclick Trainer has a beige color, and contains no medicine and no needle.
- Your auto-injector is designed to work through clothing.
- The two blue end caps on the Adrenaclick auto-injector help to prevent accidental injection of the device. Do not remove the blue end caps 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 red tip. The needle comes out of the red tip.
- If an accidental injection happens, get medical help right away.
- Do not place patient information or any other foreign objects in carrier with the auto-injector, as this may prevent you from removing the auto-injector for use.

Instructions for Use

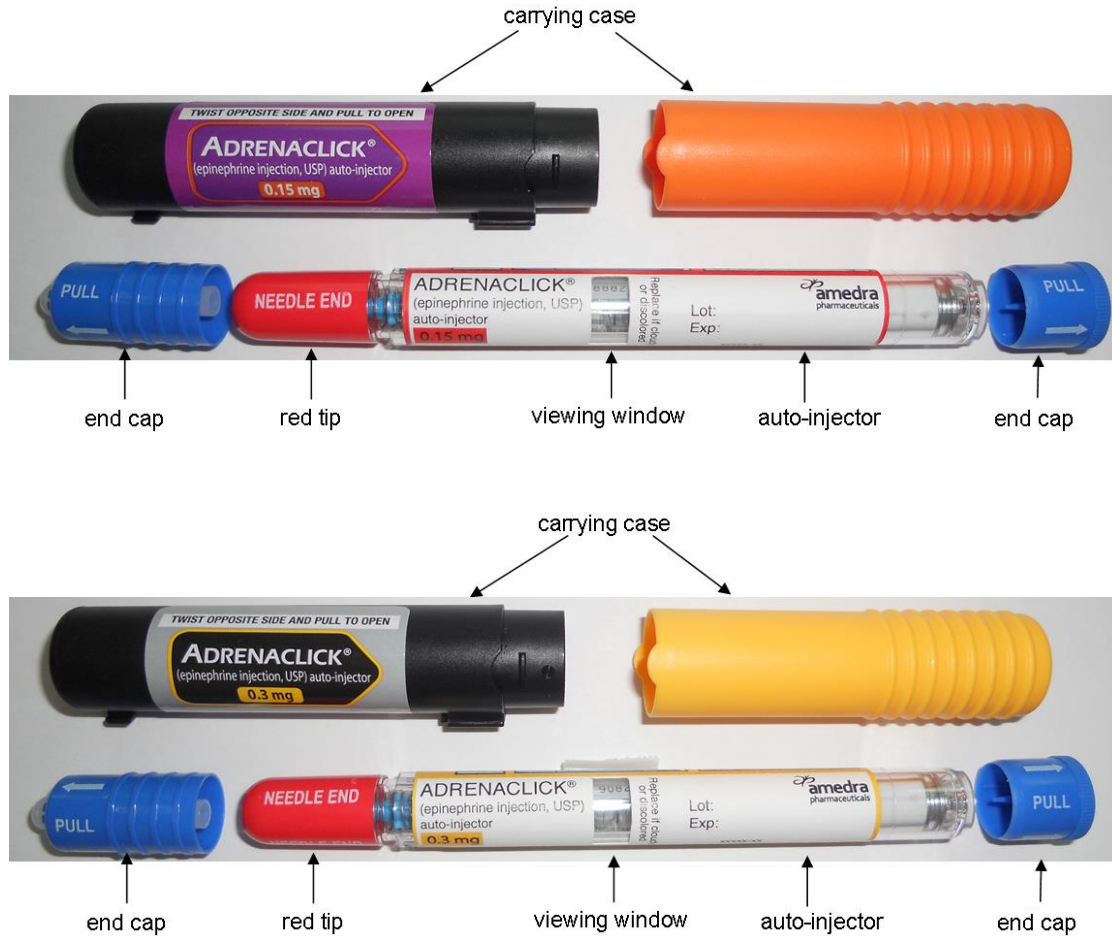
ADRENACLICK[®] (a-dren-a-click)

(epinephrine injection) auto-injector

For allergic emergencies (anaphylaxis)

Read these Instructions for Use carefully before you use Adrenaclick. Before you need to use your Adrenaclick, 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 Adrenaclick auto-injector should also understand how to use it well. If you have any questions, ask your healthcare provider.

Your Adrenaclick auto-injector



STEP 1. Prepare Adrenaclick for injection

- Remove Adrenaclick from its protective carrying case.
- **Pull off blue end caps**; you will now see a red tip. Grasp the auto-injector in your fist with the red tip pointing downward. **See Figure A.**

Note:

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

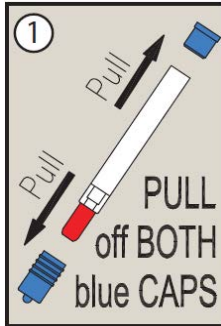


Figure A

STEP 2. Administer AdrenaClick

- **Put the red tip against the middle of the outer thigh** (upper leg) at a 90° angle (perpendicular) to the thigh.
- **Press down hard and hold firmly against the thigh for approximately 10 seconds** to deliver the medicine. See [Figure B](#).

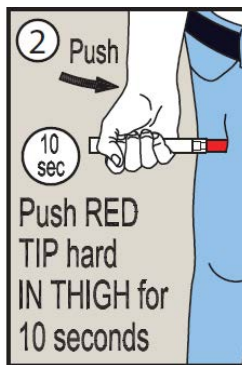


Figure B

- Only inject into the middle of the outer thigh. **Do not** inject into any other part of the body.
- **Remove AdrenaClick from the thigh.**
- Massage the area for 10 seconds.
- **Check the red tip.** The injection is complete and you have received the correct dose of the medicine if you see the needle sticking out of the **red tip**. **If you do not see the needle repeat Step 2.**

STEP 3. Get emergency medical help right away. You may need further medical attention. You may need to use a second Adrenaclick auto-injector if symptoms continue or recur.

STEP 4. After use / Disposal

Carefully cover the needle with the carrying case.

- Lay the labeled half of the carrying case cover down on a flat surface. Use one hand to carefully slide the end of the auto-injector, needle first, into the labeled carrying case cover. **See Figure C.**

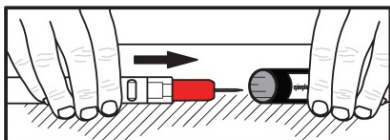


Figure C

- After the needle is inside the labeled cover, push the unlabeled half of the carrying case cover firmly over the non-needle end of the auto-injector. **See Figure D.**

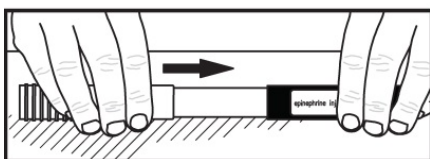


Figure D

- Take your used Adrenaclick 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 Adrenaclick auto-injector to the healthcare provider for inspection and proper disposal.
- Ask for a refill, if needed.

Note:

- Adrenaclick is a single-use injectable device that delivers a fixed dose of epinephrine. The auto-injector cannot be reused. 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 you see the needle sticking out of the **red** tip.
- A separate Adrenaclick Trainer is available. The Adrenaclick Trainer has a beige color. The beige Adrenaclick Trainer contains no medicine and no needle. Practice with your Adrenaclick Trainer, but always carry your real Adrenaclick auto-injector in case of an allergic emergency.
- Do not try to take the Adrenaclick auto-injector apart.

This label may not be the latest approved by FDA.
For current labeling information, please visit <https://www.fda.gov/drugsatfda>

For more information and video instructions on the use of Adrenaclick, go to www.adrenaclick.com or call 1-888-894-6528.

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

10/2014

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Amedra Pharmaceuticals LLC

Horsham, PA 19044

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(b) (4)

PRINT VIEW
 DIE 5195

ADRENACLICK®
 (epinephrine injection, USP) auto-injector
0.3 mg

Each 0.3 mL contains:
 0.3 mg epinephrine
 2.6 mg sodium chloride
 0.45 mg sodium bisulfite

not more than 1.5 mg chlorobutanol hydrochloric acid and sodium hydroxide to adjust pH water for injection

ADRENACLICK®
 (epinephrine injection, USP) auto-injector
0.3 mg

Two-Pack
 One 0.3 mg dose in each Adrenaclick® Auto-Injector

See enclosed Patient Information Leaflet for complete instructions for use.

1 Pull off BOTH blue CAPS

2 Push

10 sec

Push RED TIP hard IN THIGH for 10 seconds

3 SEEK MEDICAL ATTENTION

4 First slide needle into labeled half of carrying case. Close Case.

Note: The needle comes out of the red tip. Never put your thumb, fingers, or hand over the red tip.

- Protect from heat or light
- Do not refrigerate
- Replace auto-injector if solution is discolored, cloudy, or contains particles
- Store at room temperature 68°-77°F (20°-25°C); excursions permitted to 59°-86°F (15°-30°C)

Distributed by:
 Amedra Pharmaceuticals LLC
 Horsham, PA 19044 USA

Additional training is available at www.adrenaclick.com
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FPO

3 52054 80402 2

ADRENACLICK®

0.3 mg

(epinephrine injection, USP) auto-injector

Contains TWO Adrenaclick® 0.3 mg Auto-Injectors

Rx Only

For Subcutaneous or Intramuscular Use Only

For Allergic Emergencies (Anaphylaxis)

Distributed by:
 amedra pharmaceuticals
 Amedra Pharmaceuticals LLC
 Horsham, PA 19044 USA

NDC 52054-804-02
Two-Pack

ADRENACLICK®

0.3 mg

(epinephrine injection, USP) auto-injector

XXXXX-XX

IMPORTANT Read instructions for Use carefully before use
 For intramuscular or subcutaneous use For allergic emergencies (anaphylaxis)
 Each 0.3 mL contains 0.3 mg epinephrine 2.6 mg sodium chloride
 0.45 mg sodium bisulfite no more than 1.5 mg chlorobutanol
 Store at 20°C-25°C (68°F-77°F) with excursions permitted to 15°C-30°C (59°-86°F)
 Protect from light Do not refrigerate Rx only
 Distributed by Amedra Pharmaceuticals LLC Horsham PA 19044
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XXXXXX-XX

0.3 mg
 (epinephrine injection, USP) auto-injector

Replace if cloudy or discolored

Exp:
 Lot:

ADRENALIN[®]
 amedra pharmaceuticals

1 PULL BOTH off BOTH blue CAPS

2 Push **10** seconds **PUSH RED TIP hard IN THIGH for 10 seconds**

3 SEEK MEDICAL ATTENTION

Peel here for further instructions.

4 After Use / Disposal

Lay labeled half of carrying case on flat surface. Carefully slide needle end of auto-injector into labeled carrying case cover.

Push unlabeled half of carrying case firmly over non-needle end of auto-injector.

Give used auto-injector to healthcare provider for proper disposal.



(b) (4)

IMPORTANT Read instructions for Use carefully before use
 For intramuscular or subcutaneous use For allergic emergencies (anaphylaxis)
 Each 0.15 mL contains 0.15 mg epinephrine, 1.3 mg sodium chloride,
 0.225 mg sodium bisulfite, no more than 0.75 mg chlorobutanol
 Store at 20°C to 25°C (68°F to 77°F) with excursions permitted to 15°C to 30°C (59° to 86°F)
 Protect from light. Do not refrigerate. Rx only.
 Distributed by Amedra Pharmaceuticals LLC, Horsham, PA 19044
 © 2014 Amedra Pharmaceuticals LLC, Horsham, PA 19044

ADRENACLIK® (epinephrine injection, USP) 0.15 mg auto-injector

Replace if cloudy or discolored

Exp: Lot: XXXXX-XX

ameda pharmaceuticals

- 1** PULL off BOTH blue CAPS
- 2** Push **10 sec** PUSH RED TIP hard IN THIGH for 10 seconds
- 3** SEEK MEDICAL ATTENTION
Peel here for further instructions

4 After Use / Disposal

Lay labeled half of carrying case on flat surface. Carefully slide needle end of auto-injector into labeled carrying case cover.

Push unlabeled half of carrying case on firmly over non-needle end of auto-injector.

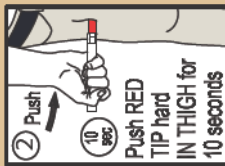
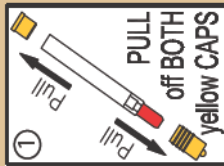
Give used auto-injector to healthcare provider for proper disposal.

TRAINER

IMPORTANT: TRAINER contains no needle or drug product
Read instructions and become familiar with TRAINER prior to use.

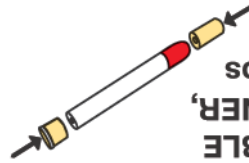
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TRAINER CONTAINS NO NEEDLE OR DRUG PRODUCT
FOR PRACTICE ONLY
REUSABLE
Lot: _____
1516 XX
(epinephrine injector, USP) auto-injector
for ADRENALIN[®]

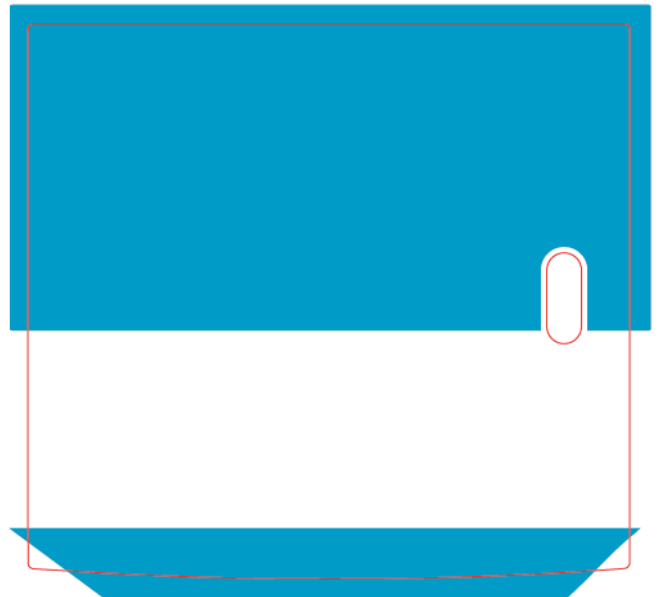
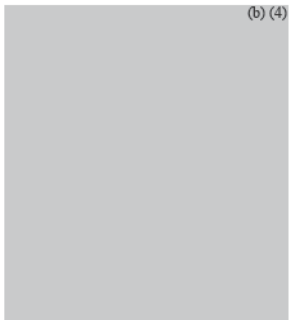


3 Contains no needle or drug

Peel here for further instructions



TRAINER is REUSABLE
To reassemble TRAINER,
Reapply yellow caps



ADHESIVE

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use EPINEPHRINE INJECTION, USP AUTO-INJECTOR safely and effectively. See full prescribing information for EPINEPHRINE INJECTION, USP AUTO-INJECTOR.

Epinephrine injection, USP auto-injector 0.3 mg, 0.15 mg, for intramuscular or subcutaneous use
Initial U.S. Approval: 1939

INDICATIONS AND USAGE

Epinephrine injection, USP auto-injector contains 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): Epinephrine injection, USP auto-injector 0.3 mg (2)
- Patients 15 to 30 kg (33 lbs-66 lbs): Epinephrine injection, USP auto-injector 0.15 mg (2)

Inject epinephrine injection, USP auto-injector 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

- Injection, 0.3 mg: 0.3 mg/0.3 mL epinephrine injection, USP, pre-filled auto-injector (3)
- Injection, 0.15 mg: 0.15 mg/0.15 mL epinephrine injection, 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)
- The presence of a sulfite in this product should not deter use. (5.3)
- Administer with caution in patients with heart disease; may aggravate angina pectoris or produce ventricular arrhythmias. (5.4)

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 Lineage Therapeutics Inc. at 1-888-894-6528 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. (5.4, 8.5)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 10/2014

FULL PRESCRIBING INFORMATION: CONTENTS*

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2	DOSAGE AND ADMINISTRATION		
3	DOSAGE FORMS AND STRENGTHS		
4	CONTRAINDICATIONS		
5	WARNINGS AND PRECAUTIONS		
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	5.2	Incorrect Locations of Injection	
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*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Epinephrine injection, USP auto-injector is indicated in the emergency treatment of allergic reactions (Type I) including anaphylaxis to stinging insects (e.g., order Hymenoptera, which includes 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.

Epinephrine injection, USP auto-injector is 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.

Epinephrine injection, USP auto-injector is intended for immediate administration as emergency supportive therapy only and is not a replacement or substitute for immediate medical care.

2 DOSAGE AND ADMINISTRATION

Selection of the appropriate epinephrine injection, USP auto-injector dosage strength is determined according to patient body weight.

- Patients greater than or equal to 30 kg (approximately 66 pounds or more): epinephrine injection, USP auto-injector 0.3 mg
- Patients 15 to 30 kg (33 pounds to 66 pounds): epinephrine injection, USP auto-injector 0.15 mg

Inject epinephrine injection, USP auto-injector intramuscularly or subcutaneously into the anterolateral aspect of the thigh, through clothing if necessary.

Each epinephrine injection, USP auto-injector contains a single dose of epinephrine for single use injection. Since the doses of epinephrine delivered from epinephrine injection, USP 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 epinephrine injection, USP auto-injector 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 viewing window of epinephrine injection, USP auto-injector should be inspected visually for particulate matter and discoloration. Epinephrine is light sensitive and should be stored in the outer case provided to protect it from light [*see How Supplied/Storage and Handling (16.2)*].

3 DOSAGE FORMS AND STRENGTHS

- Injection, 0.3 mg/0.3 mL epinephrine injection, USP, pre-filled auto-injector
- Injection, 0.15 mg/0.15 mL epinephrine injection, USP, pre-filled auto-injector

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Emergency Treatment

Epinephrine injection, USP auto-injector is intended for immediate administration as emergency supportive therapy and is 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 Incorrect Locations of Injection

Epinephrine injection, USP auto-injector 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 a 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 the development of gas gangrene. Cleansing with alcohol does not kill bacterial spores, and therefore, does not lower the 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)*].

5.3 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 bisulfite, 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.

5.4 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 epinephrine injection, USP auto-injector 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 (5.4)*].

Arrhythmias, including fatal ventricular fibrillation, have been reported, particularly in patients with underlying cardiac disease or those receiving certain drugs [*see Warnings and Precautions (5.4) and Drug Interactions (7)*].

Rapid rises in blood pressure have produced cerebral hemorrhage, particularly in elderly patients with cardiovascular disease [*see Warnings and Precautions (5.4)*].

Angina may occur in patients with coronary artery disease [*see Warnings and Precautions (5.4)*].

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.

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

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 (5.4)*].

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/m^2 basis at a maternal dose of 1.2 $\text{mg}/\text{kg}/\text{day}$ for two to three days), in mice at approximately 7 times the maximum daily subcutaneous or intramuscular dose (on a mg/m^2 basis at a maternal subcutaneous dose of 1 $\text{mg}/\text{kg}/\text{day}$ for 10 days), and in hamsters at approximately 5 times the maximum recommended daily subcutaneous or intramuscular dose (on a mg/m^2 basis at a maternal subcutaneous dose of 0.5 $\text{mg}/\text{kg}/\text{day}$ 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/m^2 basis at a subcutaneous maternal dose of 0.5 $\text{mg}/\text{kg}/\text{day}$ 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 epinephrine injection, USP auto-injector is administered to a nursing woman.

8.4 Pediatric Use

Epinephrine injection, USP auto-injector 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 dose of epinephrine delivered from epinephrine injection, USP auto-injector is 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, epinephrine injection, USP auto-injector 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 (5.4) and 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 a rapidly acting vasodilators or alpha-adrenergic blocking drugs and/or respiratory support.

Epinephrine overdose 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

Epinephrine injection, USP auto-injector 0.3 mg and 0.15 mg is an auto-injector and a combination product containing drug and device components.

Each epinephrine injection, USP auto-injector 0.3 mg delivers a single dose of 0.3 mg epinephrine from epinephrine injection, USP (0.3 mL) in a sterile solution.

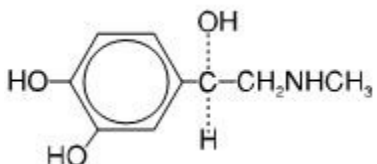
Each epinephrine injection, USP auto-injector 0.15 mg delivers a single dose of 0.15 mg epinephrine from epinephrine injection, USP (0.15 mL) in a sterile solution.

Epinephrine injection, USP auto-injector 0.3 mg and epinephrine injection, USP auto-injector 0.15 mg each contain 1.1 mL of epinephrine solution. 0.3 mL and 0.15 mL epinephrine solution are dispensed for epinephrine injection, USP auto-injector 0.3 mg and epinephrine injection, USP auto-injector 0.15 mg, respectively, when activated. The solution remaining after activation is not available for future use and should be discarded.

Each 0.3 mL in epinephrine injection, USP auto-injector 0.3 mg contains 0.3 mg epinephrine, 2.6 mg sodium chloride, not more than 1.5 mg chlorobutanol, 0.45 mg sodium bisulfite, hydrochloric acid and sodium hydroxide to adjust pH, and water for injection. The pH range is 2.2-5.0.

Each 0.15 mL in epinephrine injection, USP auto-injector 0.15 mg contains 0.15 mg epinephrine, 1.3 mg sodium chloride, not more than 0.75 mg chlorobutanol, 0.225 sodium bisulfite, hydrochloric acid and sodium hydroxide 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 epinephrine injection, USP

auto-injector if the epinephrine solution appears discolored (pinkish or brown color), cloudy, or contains particles.

Thoroughly review the patient instructions and operation of epinephrine injection, USP auto-injector 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 intramuscularly or subcutaneously, 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

Carton containing two epinephrine injection, USP auto-injectors 0.3 mg: NDC 54505-102-02.

Carton containing one epinephrine injection, USP auto-injector 0.3 mg: NDC 54505-102-01.

Carton containing two epinephrine injection, USP auto-injectors 0.15 mg: NDC 54505-101-02.

Carton containing one epinephrine injection, USP auto-injector 0.15 mg: NDC 54505-101-01.

Rx only

16.2 Storage and Handling

Protect from light. Epinephrine is light sensitive and should be stored in the carrying-case provided to protect it from light. Store at room temperature (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 epinephrine injection, USP auto-injector, 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

Patients and/or caregivers should be instructed in the appropriate use of epinephrine injection, USP auto-injector. Epinephrine injection, USP auto-injector should be injected into the middle of the outer thigh (through clothing if necessary). Each epinephrine injection, USP auto-injector is a single-use injection. Advise patients to seek immediate medical care in conjunction with administration of epinephrine injection, USP auto-injector.

Complete patient information, including dosage, directions for proper administration and precautions can be found inside each epinephrine injection, USP auto-injector carton. A printed label on the surface of epinephrine injection, USP auto-injector shows instructions for use and a diagram depicting the injection process.

Patients and/or caregivers should be instructed to use the Trainer to familiarize themselves with the use of epinephrine injection, USP auto-injector in an allergic emergency. The Trainer may be used multiple times.

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 (5.4)*].

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 vasodilation if there is such an accidental injection to these areas [*see Warnings and Precautions (5.2)*].

Storage and Handling

Instruct patients to inspect the epinephrine solution visually through the viewing window periodically. Epinephrine injection, USP auto-injector should be replaced if the epinephrine solution appears discolored (pinkish or brown), cloudy, or contains particles. Epinephrine is light sensitive and should be stored in the outer case provided to protect it from light. Patients should be instructed that epinephrine injection, USP auto-injector must be properly disposed of once the blue caps have been removed or after use [*see How Supplied/Storage and Handling (16.2)*].

Complete patient information, including dosage, directions for proper administration and precautions are provided inside each epinephrine injection, USP auto-injector carton.

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For inquiries call 1-888-894-6528

71006-07

Patient Information

EPINEPHRINE INJECTION, USP AUTO-INJECTOR (ep-in-eph-rine)

Authorized generic of Adrenaclick®

For allergic emergencies (anaphylaxis)

Read this Patient Information Leaflet carefully before you use the epinephrine injection, USP 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 epinephrine injection, USP 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 epinephrine injection, USP auto-injector?

1. Epinephrine injection, USP auto-injector contains 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 other unknown causes.

Symptoms of an 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 epinephrine injection, USP auto-injector 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 epinephrine injection, USP auto-injector 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 epinephrine injection, USP auto-injector right away.**
 - **Get emergency medical help right away.** You may need further medical attention. You may need to use a second epinephrine injection, USP auto-injector 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 is epinephrine injection, USP auto-injector?

- Epinephrine injection, USP auto-injector is a disposable, prefilled automatic injection device (auto-injector) 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.
- Epinephrine injection, USP auto-injector is for immediate self (or caregiver) administration and does not take the place of emergency medical care. You should get emergency medical help right away after using epinephrine injection, USP auto-injector.
- Epinephrine injection, USP auto-injector is for people who have been prescribed this medicine by their healthcare provider.
- The epinephrine injection, USP auto-injector 0.3 mg auto-injector is for patients who weigh 66 pounds or more (30 kilograms or more).
- The epinephrine injection, USP auto-injector 0.15 mg auto-injector is for patients who weigh about 33 to 66 pounds (15 to 30 kilograms).
- It is not known if epinephrine injection, USP auto-injector is safe and effective in children who weigh less than 33 pounds (15 kilograms).

What should I tell my healthcare provider before using epinephrine injection, USP auto-injector?

Before you use epinephrine injection, USP auto-injector, tell your healthcare provider about all your medical conditions, 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.

Epinephrine injection, USP auto-injector and other medicines may affect each other, causing side effects. Epinephrine injection, USP auto-injector may affect the way other medicines work, and other medicines may affect how epinephrine injection, USP auto-injector works.

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 epinephrine injection, USP auto-injector for treatment of anaphylaxis as prescribed by your healthcare provider, regardless of your medical conditions or the medicine you take.

How should I use epinephrine injection, USP auto-injector?

- Each epinephrine injection, USP auto-injector contains only 1 dose of medicine.
- Epinephrine injection, USP auto-injector should only be injected into the middle of the outer thigh (upper leg). It can be injected through clothing, if needed.
- Read the Instructions for Use at the end of this Patient Information Leaflet for information about the right way to use epinephrine injection, USP auto-injector.
- Your healthcare provider will show you how to safely use the epinephrine injection, USP auto-injector.
- Use epinephrine injection, USP auto-injector exactly as your healthcare provider tells you to use it. You may need to use a second epinephrine injection, USP auto-injector 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 red tip. Never press or push the red tip with your thumb, fingers, or hand.** The needle comes out of the red tip. Accidental injection into finger, hands, or feet may cause a loss of blood flow to those 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 epinephrine injection, USP auto-injector comes packaged in a carton containing 1 or 2 epinephrine injection, USP auto-injectors.
- You may request a separate Trainer, that comes packaged with Trainer Instructions for Use. Additional video instructions on the use of epinephrine injection, USP auto-injector are available from www.epinephrineautoinject.com. **The epinephrine injection, USP auto-injector Trainer has a beige color. The beige epinephrine injection, USP auto-injector Trainer contains no medicine and no needle.** Practice with your epinephrine injection, USP auto-injector Trainer before an allergic emergency happens to make sure you are able to safely use the real epinephrine injection, USP auto-injector in an emergency. Always carry your real epinephrine injection, USP auto-injector with you in case of an allergic emergency.
- Do not drop the carrying case or epinephrine injection, USP auto-injector. If the carrying case or epinephrine injection, USP auto-injector is dropped, check for damage and leakage. Dispose of the auto-injector and carrying case, and replace if damage or leakage is noticed or suspected.

What are the possible side effects of epinephrine injection, USP auto-injector?

Epinephrine injection, USP auto-injector may cause serious side effects.

- **Epinephrine injection, USP auto-injector should only be injected into the middle of your outer thigh (upper leg).** Do not inject epinephrine injection, USP auto-injector into your:
 - veins
 - buttocks
 - fingers, toes, hands or feet.

If you accidentally inject epinephrine injection, USP auto-injector 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.

- **If you have certain medical conditions, or take certain medicines, your condition may get worse or you may have more or longer lasting side effects when you use epinephrine injection, USP auto-injector.** Talk to your healthcare provider about all your medical conditions.

Common side effects of epinephrine injection, USP auto-injector include:

- faster, 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 epinephrine injection, USP auto-injector. 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 epinephrine injection, USP auto-injector?

- Store epinephrine injection, USP auto-injector at room temperature between 68° to 77° F (20° to 25° C).
- Protect from light.
- **Do not** expose to extreme heat or cold. 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 viewing window of your auto-injector periodically. The solution should be clear. If the solution is discolored (pinkish or brown), cloudy or contains solid particles, replace the unit.
- Always keep your epinephrine injection, USP auto-injector in the carrying case to protect it from damage; however, the carrying case is not waterproof.
- The two blue end caps help to prevent accidental injection. Do not remove the blue end caps until you are ready to use epinephrine injection, USP auto-injector.
- Your epinephrine injection, USP auto-injector has an expiration date. Replace it before the expiration date.

Keep epinephrine injection, USP auto-injector and all medicines out of the reach of children.

General information about the safe and effective use of epinephrine injection, USP auto-injector:

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information Leaflet. Do not use epinephrine injection, USP auto-injector for

a condition for which it was not prescribed. Do not give epinephrine injection, USP auto-injector to other people.

This Patient Information Leaflet summarizes the most important information about epinephrine injection, USP auto-injector. If you would like more information, talk to your healthcare provider. You can ask your pharmacist or healthcare provider for information about epinephrine injection, USP auto-injector that is written for health professionals.

For more information and video instructions on the use of epinephrine injection, USP auto-injector, go to www.epinephrineautoinject.com or call 1-888-894-6528.

What are the ingredients in epinephrine injection, USP auto-injector?

Active Ingredient: epinephrine

Inactive Ingredients: sodium chloride, chlorobutanol, sodium bisulfite, hydrochloric acid and sodium hydroxide, and water.

Important Information

- **The epinephrine injection, USP auto-injector 0.3 mg auto-injector has a yellow colored label.**
- **The epinephrine injection, USP auto-injector 0.15 mg auto-injector has an orange colored label.**
- **The epinephrine injection, USP auto-injector Trainer has a beige color, and contains no medicine and no needle.**
- **Your auto-injector is designed to work through clothing.**
- **The two blue end caps on the epinephrine injection, USP auto-injector help to prevent accidental injection of the device. Do not remove the blue end caps 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 red tip. The needle comes out of the red tip.**
- **If an accidental injection happens, get medical help right away.**
- **Do not place patient information or any other foreign objects in carrier with the auto-injector, as this may prevent you from removing the auto-injector for use.**

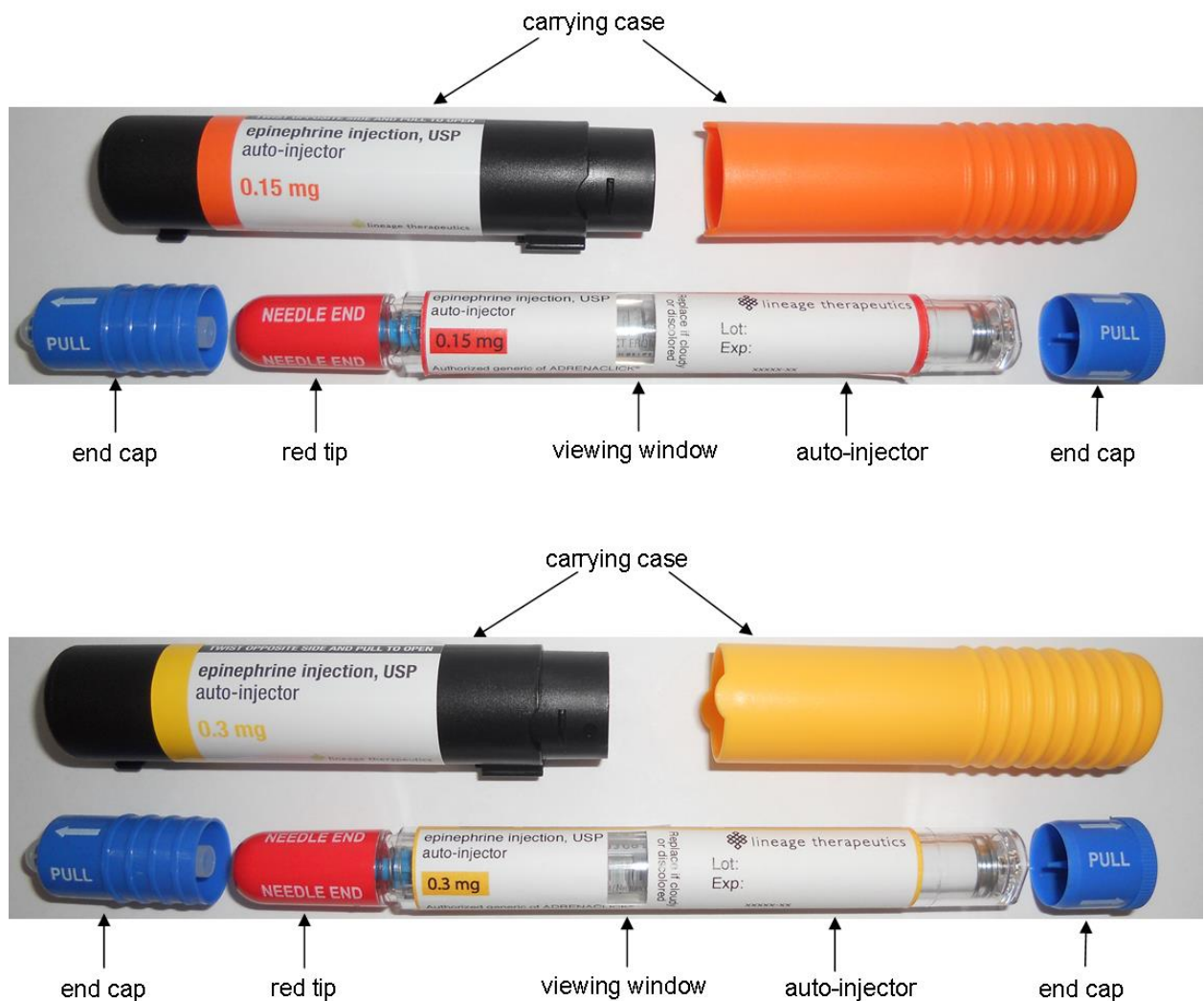
Instructions for Use

EPINEPHRINE INJECTION, USP AUTO-INJECTOR (ep-in-eph-rine)

For allergic emergencies (anaphylaxis)

Read these Instructions for Use carefully before you use epinephrine injection, USP auto-injector. Before you need to use your epinephrine injection, USP auto-injector, 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 epinephrine injection, USP auto-injector should also understand how to use it well. If you have any questions, ask your healthcare provider.

Your epinephrine injection, USP auto-injector



STEP 1. Prepare epinephrine injection, USP auto-injector for injection

- Remove epinephrine injection, USP auto-injector from its protective carrying case.
- **Pull off blue end caps**; you will now see a red tip. Grasp the auto-injector in your fist with the red tip pointing downward. See **Figure A**.

Note:

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

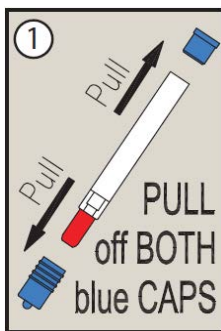


Figure A

STEP 2. Administer epinephrine injection, USP auto-injector

- **Put the red tip against the middle of the outer thigh** (upper leg) at a 90° angle (perpendicular) to the thigh.
- **Press down hard and hold firmly against the thigh for approximately 10 seconds** to deliver the medicine. See **Figure B**.



Figure B

- Only inject into the middle of the outer thigh. **Do not** inject into any other part of the body.
- **Remove epinephrine injection, USP auto-injector from the thigh.**
- Massage the area for 10 seconds.
- **Check the red tip.** The injection is complete and you have received the correct dose of the medicine if you see the needle sticking out of the **red tip**. **If you do not see the needle repeat Step 2.**

STEP 3. Get emergency medical help right away. You may need further medical attention. You may need to use a second epinephrine injection, USP auto-injector if symptoms continue or recur.

STEP 4. After use / Disposal

Carefully cover the needle with the carrying case.

- Lay the labeled half of the carrying case cover down on a flat surface. Use one hand to carefully slide the end of the auto-injector, needle first, into the labeled carrying case cover. **See Figure C.**

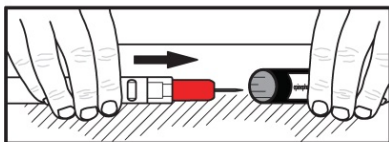


Figure C

- After the needle is inside the labeled cover, push the unlabeled half of the carrying case cover firmly over the non-needle end of the auto-injector. **See Figure D.**

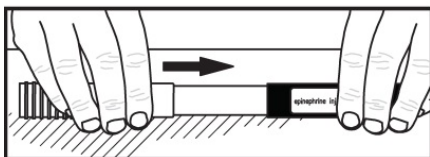


Figure D

- Take your used epinephrine injection, USP 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 epinephrine injection, USP auto-injector to the healthcare provider for inspection and proper disposal.
- Ask for a refill, if needed.

Note:

- Epinephrine injection, USP auto-injector is a single-use injectable device that delivers a fixed dose of epinephrine. The auto-injector cannot be reused. 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 you see the needle sticking out of the **red** tip.
- A separate epinephrine injection, USP auto-injector Trainer is available. The epinephrine injection, USP auto-injector Trainer has a beige color. The beige epinephrine injection, USP auto-injector Trainer contains no medicine and no needle. Practice with your epinephrine injection, USP auto-injector Trainer, but always carry your real epinephrine injection, USP auto-injector in case of an allergic emergency.
- Do not try to take the epinephrine injection, USP auto-injector apart.

For more information and video instructions on the use of epinephrine injection, USP auto-injector, go to www.epinephrineautoinject.com or call 1-888-894-6528.

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

10/2014

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Horsham, PA 19044

71007-07

PROOF ENTIRE LABEL

- APPROVED: OK TO PRINT CHANGES REQUIRED: SUBMIT ADDITIONAL PROOFS
 OK FOR FDA SUBMISSION ONLY

AUTHORIZED BY: _____

DATE: _____ Production delivery 2-3 weeks from receipt of OK TO PRINT.

lineage therapeutics
epinephrine injection, USP
auto-injector
0.3 mg

Each 0.3 mL contains:
 0.3 mg epinephrine not more than 1.5 mg chlorobutanol
 2.6 mg sodium chloride hydrochloric acid and sodium hydroxide to adjust pH
 0.45 mg sodium bisulfite water for injection

1 Pull off BOTH blue CAPS

2 Push
 Push RED TIP hard IN THIGH for 10 seconds

3 SEEK MEDICAL ATTENTION

4 First slide needle into labeled half of carrying case. Close Case.

Note: The needle comes out of the red tip. Never put your thumb, fingers, or hand over the red tip.

See enclosed Patient Information Leaflet for complete instructions for use.

Protect from heat or light
 Do not refrigerate
 Replace auto-injector if solution is discolored, cloudy, or contains particles

Store at room temperature 68°-77°F (20°-25°C); excursions permitted to 59°-86°F (15°-30°C)

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lineage therapeutics
epinephrine injection, USP
auto-injector
0.3 mg

For more information, scan QR Code

or visit
epinephrineautoinject.com

lineage therapeutics
epinephrine injection, USP
auto-injector
0.3 mg

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lineage therapeutics
epinephrine injection, USP
auto-injector
0.3 mg

FOR ALLERGIC EMERGENCES
 In patients weighing over 66 lb
 For Subcutaneous or Intramuscular
 Use Only

0.3 mg
auto-injector
epinephrine injection, USP
lineage therapeutics

Rx only
 NDC 54505-102-02

This carton contains:
 Two epinephrine auto-injectors

For information, please visit
epinephrineautoinject.com
 Authorized generic of Adrenalick®

Made in the USA

lineage therapeutics
epinephrine injection, USP
auto-injector
0.3 mg

No Coating Area not to exceed this box

Die Cut

NOTES: We changed NDC # to read 54505-102-02 to match NDC # and 1 Pack carton

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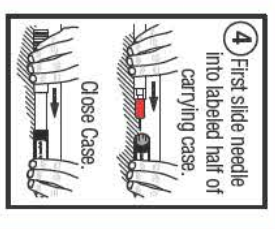
AUTHORIZED BY: _____

DATE: _____ Production delivery 2-3 weeks from receipt of OK TO PRINT.


lineage therapeutics
epinephrine injection, USP
auto-injector
0.15 mg

Each 0.15 mL contains:
 0.15 mg epinephrine
 1.3 mg sodium chloride
 0.225 mg sodium bisulfite


not more than 0.75 mg chlorobutanol hydrochloric acid and sodium hydroxide to adjust pH water for injection



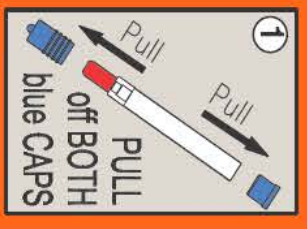
4 First slide needle into labeled half of carrying case. Close Case.



3 SEEK MEDICAL ATTENTION



2 Push
 Push RED TIP hard IN THIGH for 10 seconds



1 Pull
 Pull off BOTH blue CAPS

Note: The needle comes out of the red tip. Never put your thumb, fingers, or hand over the red tip.

See enclosed Patient Information Leaflet for complete instructions for use.

Protect from heat or light


Do not refrigerate

Replace auto-injector if solution is discolored, cloudy, or contains particles

Store at room temperature 68°-77°F (20°-25°C); excursions permitted to 59°-86°F (15°-30°C)


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or visit
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epinephrine injection, USP
auto-injector
0.15 mg



3 54505 10102 2

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epinephrine injection, USP
auto-injector
0.15 mg

lineage therapeutics
epinephrine injection, USP
auto-injector
0.15 mg

FOR ALLERGIC EMERGENCES
 In patients weighing 33 lb - 66 lb
 For Subcutaneous or Intramuscular Use Only

NDC 54505-101-02
 Rx only


This carton contains:
 Two epinephrine auto-injectors

For information, please visit
epinephrineautoinject.com
 Authorized generic of Adrenalick®

lineage therapeutics
epinephrine injection, USP
auto-injector
0.15 mg

Made in the USA

Lot
 Exp.



XXXXXX-XX

lineage therapeutics
epinephrine injection, USP
auto-injector
0.15 mg

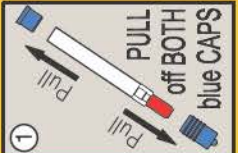


NO COATING AREA
 NOT TO EXCEED THIS BOX

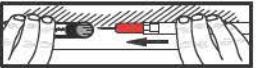

Die Cut

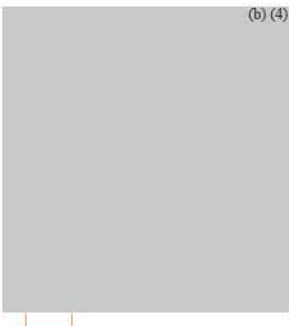
NOTES: We changed NDC # to read 54505-102-02 to match NDC # and 1 Pack carton

IMPORTANT Read instructions for Use carefully before use
 For intramuscular or subcutaneous use For allergic emergencies (anaphylaxis)
 Each 0.3 mL contains 0.3 mg epinephrine 2.6 mg sodium chloride
 0.45 mg sodium bisulfite, no more than 1.5 mg chlorobutanol
 Store at 20°C-25°C (68°F-77°F) with excursions permitted to 15°C-30°C (59°-86°F)
 Protect from light Do not refrigerate Rx only
 Distributed by Lineage Therapeutics Inc. Horsham, PA 19044
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Authorized generic of ADRENALINE[®]
 0.3 mg
 epinephrine injection, USP
 auto-injector
 Lineage Therapeutics
 Lot:
 Exp:
 xxxxxx-xx
 Replace if cloudy or discolored

- 1** PULL BOTH off BOTH blue CAPS

- 2** Push **10** seconds
 PUSH RED TIP hard IN THIGH for 10 seconds

- 3** SEEK MEDICAL ATTENTION
 Peel here for further instructions.


4 After Use / Disposal
 Lay labeled half of carrying case on flat surface. Carefully slide needle end of auto-injector into labeled carrying case cover.

 Push unlabeled half of carrying case firmly over non-needle end of auto-injector.

 Give used auto-injector to healthcare provider for proper disposal.



(b) (4)

IMPORTANT Read instructions for Use carefully before use
 For intramuscular or subcutaneous use For allergic emergencies (anaphylaxis)
 Each 0.15 mL contains 0.15 mg epinephrine 1.3 mg sodium chloride
 0.225 mg sodium bisulfite no more than 0.75 mg chlorobutanol
 Store at 20°C-25°C (68°F-77°F) with excursions permitted to 15°C-30°C (59°-86°F)
 Protect from light Do not refrigerate Rx only
 Distributed by Lineage Therapeutics Inc. Horsham, PA 19044
 © 2014 Lineage Therapeutics Inc. Horsham, PA 19044

Authorized generic of ADRENALIN[®] USP
 epinephrine injection, USP
 0.15 mg
 auto-injector

Replace if cloudy or discolored

xxxxxx-xx

Exp:

Lot:

lineage therapeutics

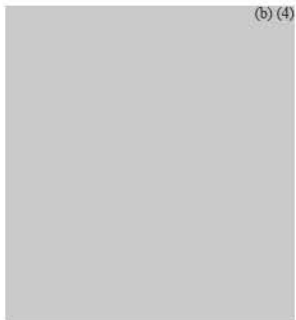
- 1** PULL off BOTH blue CAPS
- 2** Push **10** seconds
 PUSH RED TIP hard IN THIGH for 10 seconds
- 3** SEEK MEDICAL ATTENTION
 Peel here for further instructions.

4 After Use / Disposal

Lay labeled half of carrying case on flat surface. Carefully slide needle end of auto-injector into labeled carrying case cover.

Push unlabeled half of carrying case firmly over non-needle end of auto-injector.

Give used auto-injector to healthcare provider for proper disposal.



(b) (4)

NOTES: _____

APPROVED: OK TO PRINT CHANGES REQUIRED: SUBMIT ADDITIONAL PROOFS
 OK FOR FDA SUBMISSION ONLY

AUTHORIZED BY: _____

DATE: _____ Production delivery 2-3 weeks from receipt of OK TO PRINT.

TRAINER

IMPORTANT: TRAINER contains no needle or drug product
Read instructions and become familiar with TRAINER prior to use.

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Lineage Therapeutics
TRAINER
FOR PRACTICE ONLY
Lot: _____
auto-injector for the Lineage epinephrine injection, USP

TRAINER CONTAINS NO NEEDLE OR DRUG PRODUCT

① PULL off BOTH yellow CAPS

② Push
10 sec
Push RED TIP hard IN THIGH for 10 seconds

③ Contains no needle or drug

Peel here for further instructions.

FRONT

TRAINER is REUSABLE
To reassemble TRAINER, Reapply yellow caps

BACK

PROOF ENTIRE LABEL

Die Cut

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

LYDIA I GILBERT MCCLAIN
10/17/2014