

# Save up to \$30 per carton\*

**teva** | **epinephrine**  
injection USP (auto-injectors)  
0.15 mg | 0.3 mg

Expires: **6/30/2023**

**BIN 610020**

**GRP 99994248**

**PCN N/A**

**ID 63202507210**

You must present this offer and your primary insurance card to the pharmacist along with your prescription.

\* Commercially insured patients may save up to \$30 out of pocket per carton, up to a maximum of three (3) cartons per prescription. This offer is not available to non-insured/cash-paying patients, nor patients eligible for prescription coverage by any state or federally funded healthcare programs. Maximum reimbursement limits apply. Patient out-of-pocket expenses may vary.

## SAVINGS OFFER TERMS, CONDITIONS, AND ELIGIBILITY REQUIREMENTS

**Terms and Conditions:** Only commercially insured patients are eligible for this offer. Patients are not eligible for this offer if they are eligible to have prescriptions paid for in part or full by any state or federally funded programs, including but not limited to Medicare, Medicaid, Medigap, VA, DOD, TRICARE, or by private health benefit programs which reimburse for the entire cost of prescription drugs. This card is not valid for patients who are Medicare eligible and are enrolled in an employer-sponsored health plan or prescription drug benefit program for retirees (i.e., patients who are eligible for Medicare Part D but who receive a prescription drug benefit through a former employer). Cash Discount Cards and other non-insurance plans are not valid as primary under this offer. If the patient is eligible for drug benefits under any such program, the patient cannot use this offer. By redeeming this card, the patient (for a minor, the patient's parent or guardian) acknowledges that the patient is eligible and understands and agrees to comply with the terms and conditions of this offer.

Void if copied, transferred, purchased, altered, or traded and where prohibited and restricted by law. This is not an insurance program. This offer is limited to one per customer and may not be used with any other discount, coupon, or offer. **This offer expires on 6/30/2023. This program is managed by TrialCard on behalf of Teva Pharmaceuticals USA, Inc. Teva reserves the right to limit, change, or discontinue this offer at any time without notice.** If you have any questions regarding your eligibility or benefits, please call 844-248-7949.

**To the Patient:** This card must be presented to the Pharmacist along with your Epinephrine Auto-Injector 2-Pack prescription to participate in this program.

**Offer valid only for the following National Drug Codes:**

0.15 mg/0.3 mL - 00093-5985-27 (2-Pack)

0.3 mg/0.3 mL - 00093-5986-27 (2-Pack)

**Commercially Insured Patients:** Commercially insured patients with coverage for the Epinephrine Auto-Injector 2-Pack may save as much as \$30 on out-of-pocket expenses for each Epinephrine Auto-Injector 2-Pack carton, up to a maximum of three (3) cartons per prescription. Teva will pay up to \$30 per carton of your co-payment or cost-sharing obligation per fill. Maximum reimbursement limits apply and patient out-of-pocket expenses may vary.

**Cash-Paying Patients: Non-Insured/Cash-Paying Patients are not eligible for this offer.**

**To the Pharmacist:** By redeeming this offer, the Pharmacist certifies that the Epinephrine Auto-Injector 2-Pack is being dispensed to a patient eligible for this offer in compliance with these terms and conditions, and the Pharmacist has not submitted and will not submit a claim for reimbursement under any federal, state, or other governmental program for this prescription. Void where prohibited by law.

**Pharmacy Instructions for Commercially Insured Patients:** Please submit this claim to the primary Payer first, then submit the balance due to TrialCard as a Secondary Payer COB (coordination of benefits) with patient responsibility and a valid Other Coverage Code (e.g. 8). For each Epinephrine Auto-Injector 2-Pack carton, Teva will pay up to \$30 per carton, up to a maximum of three (3) cartons per prescription. Reimbursement will be received from TrialCard.

**Pharmacy Instructions for Uninsured Cash-Paying Patients: Cash-Paying Patients are not eligible for this offer.**

Valid Other Coverage Code required. For questions about processing, please call 844-248-7949.

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use EPINEPHRINE INJECTION, 0.3 mg and EPINEPHRINE INJECTION, 0.15 mg safely and effectively. See full prescribing information for EPINEPHRINE INJECTION, 0.3 mg and EPINEPHRINE INJECTION, 0.15 mg.

EPINEPHRINE injection, 0.3 mg, for intramuscular or subcutaneous use

EPINEPHRINE injection, 0.15 mg, for intramuscular or subcutaneous use

Initial U.S. Approval: 1939

### INDICATIONS AND USAGE

Epinephrine Injection, 0.3 mg and Epinephrine Injection, 0.15 mg contain epinephrine, are 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, 0.3 mg (2)
  - Patients 15 to 30 kg (33 lbs to 66 lbs): Epinephrine injection, 0.15 mg (2)
- Inject intramuscularly or subcutaneously into the anterolateral aspect of the thigh, through clothing if necessary. Each device is a single-dose injection. (2)

### DOSAGE FORMS AND STRENGTHS

- Injection: 0.3 mg (0.3 mg/0.3 mL) single-dose pre-filled auto-injector (3)
- Injection: 0.15 mg (0.15 mg/0.3 mL) single-dose pre-filled auto-injector (3)

### CONTRAINDICATIONS

None (4)

### WARNINGS AND PRECAUTIONS

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

### ADVERSE REACTIONS

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

To report SUSPECTED ADVERSE REACTIONS, contact Teva Pharmaceuticals USA, Inc. at 1-888-838-2872 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

### DRUG INTERACTIONS

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

### USE IN SPECIFIC POPULATIONS

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

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

Revised: 1/2021

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## FULL PRESCRIBING INFORMATION

### 1 INDICATIONS AND USAGE

Epinephrine Injection, 0.3 mg and Epinephrine Injection, 0.15 mg are indicated in the emergency treatment of allergic reactions (Type I) including anaphylaxis to stinging insects (e.g., order Hymenoptera, which include bees, wasps, hornets, yellow jackets and fire ants) and biting insects (e.g., triatoma, mosquitoes), allergen immunotherapy, foods, drugs, diagnostic testing substances (e.g., radiocontrast media) and other allergens, as well as idiopathic anaphylaxis or exercise-induced anaphylaxis.

Epinephrine Injection, 0.3 mg and Epinephrine Injection, 0.15 mg are intended for immediate administration in patients who are determined to be at increased risk for anaphylaxis, including individuals with a history of anaphylactic reactions.

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

Epinephrine Injection, 0.3 mg and Epinephrine Injection, 0.15 mg are intended for immediate administration as emergency supportive therapy only and are not a substitute for immediate medical care.

### 2 DOSAGE AND ADMINISTRATION

#### 2.1 Recommended Dosage According to Patient Body Weight

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

#### 2.2 Administration Instructions

- Inject the single-dose epinephrine injection, 0.3 mg or epinephrine injection, 0.15 mg intramuscularly or subcutaneously into the anterolateral aspect of the thigh, through clothing if necessary. Do not inject intravenously, and do not inject into buttocks, into digits, hands or feet [see *Warnings and Precautions* (5.2)].
- Instruct caregivers of young children who are prescribed an epinephrine injection, 0.3 mg or epinephrine injection, 0.15 mg and who may be uncooperative and kick or move during an injection to hold the leg firmly in place and limit movement prior to and during an injection [see *Warnings and Precautions* (5.2)].

- Each epinephrine injection, 0.3 mg or epinephrine injection, 0.15 mg is a single-dose epinephrine injection for single use. Since the doses of epinephrine delivered from epinephrine injection, 0.3 mg or epinephrine injection, 0.15 mg are fixed, consider using other forms of injectable epinephrine if doses lower than 0.15 mg are deemed necessary.

- With severe persistent anaphylaxis, repeat injections with an additional epinephrine injection, 0.3 mg or epinephrine injection, 0.15 mg may be necessary. More than two sequential doses of epinephrine should only be administered under direct medical supervision [see *Warnings and Precautions* (5.1)].

- The epinephrine solution in the clear window of the Epinephrine Injection 0.3 mg (Auto-Injector) or Epinephrine Injection 0.15 mg (Auto-Injector) should be inspected visually for particulate matter and discoloration.

#### Discarding After Use:

The epinephrine injection 0.3 mg and epinephrine injection 0.15 mg each contain 1 mL epinephrine solution. Approximately 0.7 mL remains in the auto-injector after activation, but is not available for future use, and should be discarded.

### 3 DOSAGE FORMS AND STRENGTHS

- Injection: 0.3 mg (0.3 mg/0.3 mL), clear and colorless solution in single-dose pre-filled auto-injector
- Injection: 0.15 mg (0.15 mg/0.3 mL), clear and colorless solution in single-dose pre-filled auto-injector

### 4 CONTRAINDICATIONS

None

### 5 WARNINGS AND PRECAUTIONS

#### 5.1 Emergency Treatment

Epinephrine injection, 0.3 mg and epinephrine injection, 0.15 mg are intended for immediate administration as emergency supportive therapy and are not intended as a substitute for immediate medical care. **In conjunction with the administration of epinephrine, the patient should seek immediate medical or hospital care.** More than two sequential doses of epinephrine should only be administered under direct medical supervision [see *Indications and Usage* (1), *Dosage and Administration* (2) and *Patient Counseling Information* (17)].

## 5.2 Injection-Related Complications

Epinephrine injection, 0.3 mg and epinephrine injection, 0.15 mg should **only** be injected into the anterolateral aspect of the thigh [see *Dosage and Administration (2)* and *Patient Counseling Information (17)*].

### Do not inject intravenously

Large doses or accidental intravenous injection of epinephrine may result in cerebral hemorrhage due to sharp rise in blood pressure. Rapidly acting vasodilators can counteract the marked pressor effects of epinephrine if there is such inadvertent administration.

### Do not inject into buttock

Injection into the buttock may not provide effective treatment of anaphylaxis. Advise the patient to go immediately to the nearest emergency room for further treatment of anaphylaxis. Additionally, injection into the buttock has been associated with Clostridial infections (gas gangrene). Cleansing with alcohol does not kill bacterial spores, and therefore, does not lower this risk.

### Do not inject into digits, hands or feet

Since epinephrine is a strong vasoconstrictor, accidental injection into the digits, hands or feet may result in loss of blood flow to the affected area. Advise the patient to go immediately to the nearest emergency room and to inform the healthcare provider in the emergency room of the location of the accidental injection. Treatment of such inadvertent administration should consist of vasodilation, in addition to further appropriate treatment of anaphylaxis [see *Adverse Reactions (6)*].

### Hold leg firmly during injection

Lacerations, bent needles, and embedded needles have been reported when epinephrine injection, 0.3 mg and epinephrine injection, 0.15 mg have been injected into the thigh of young children who are uncooperative and kick or move during an injection. To minimize the risk of injection related injury when administering, hold the child's leg firmly in place and limit movement prior to and during injection.

## 5.3 Serious Infections at the Injection Site

Rare cases of serious skin and soft tissue infections, including necrotizing fasciitis and myonecrosis caused by Clostridia (gas gangrene), have been reported at the injection site following epinephrine injection for anaphylaxis. *Clostridium* spores can be present on the skin and introduced into the deep tissue with subcutaneous or intramuscular injection. While cleansing with alcohol may reduce presence of bacteria on the skin, alcohol cleansing does not kill *Clostridium* spores. To decrease the risk of *Clostridium* infection, do not inject epinephrine injection into the buttock [see *Warnings and Precautions (5.2)*]. Advise patients to seek medical care if they develop signs or symptoms of infection, such as persistent redness, warmth, swelling, or tenderness, at the epinephrine injection site.

## 5.4 Allergic Reactions Associated with Sulfite

The presence of a sulfite in this product should not deter administration of the drug for treatment of serious allergic or other emergency situations even if the patient is sulfite-sensitive. Epinephrine is the preferred treatment for serious allergic reactions or other emergency situations even though this product contains sodium metabisulfite, a sulfite that may, in other products, cause allergic-type reactions including anaphylactic symptoms or life-threatening or less severe asthmatic episodes in certain susceptible persons.

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

## 5.5 Disease Interactions

Some patients may be at greater risk for developing adverse reactions after epinephrine administration. Despite these concerns, it should be recognized that the presence of these conditions is not a contraindication to epinephrine administration in an acute, life-threatening situation. Therefore, patients with these conditions, and/or any other person who might be in a position to administer epinephrine injection, 0.3 mg or epinephrine injection, 0.15 mg to a patient experiencing anaphylaxis should be carefully instructed in regard to the circumstances under which epinephrine should be used.

### Patients with Heart Disease

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

### Other Patients and Diseases

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

## 6 ADVERSE REACTIONS

Due to the lack of randomized, controlled clinical trials of epinephrine for the treatment of anaphylaxis, the true incidence of adverse reactions associated with the systemic use of epinephrine is difficult to determine. Adverse reactions reported in observational trials, case reports, and studies are listed below.

Common adverse reactions to systemically administered epinephrine include anxiety; apprehensiveness; restlessness; tremor; weakness; dizziness; sweating; palpitations; pallor; nausea and vomiting; headache; and/or respiratory difficulties. These symptoms occur in some persons receiving therapeutic doses of epinephrine, but are more likely to occur in patients with hypertension or hyperthyroidism [see *Warnings and Precautions (5.5)*].

### Cardiovascular Reactions

- Arrhythmias, including fatal ventricular fibrillation, have been reported, particularly in patients with underlying cardiac disease or those receiving certain drugs [see *Warnings and Precautions (5.5)* and *Drug Interactions (7)*].
- Rapid rises in blood pressure have produced cerebral hemorrhage, particularly in elderly patients with cardiovascular disease [see *Warnings and Precautions (5.5)*].
- Angina may occur in patients with coronary artery disease [see *Warnings and Precautions (5.5)*].
- Rare cases of stress cardiomyopathy have been reported in patients treated with epinephrine.

### Reactions from Accidental Injection and/or Improper Technique

- 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 reactions experienced as a result of accidental injections may include increased heart rate, local reactions including injection site pallor, coldness and hypoesthesia or injury at the injection site resulting in bruising, bleeding, discoloration, erythema or skeletal injury.
- Lacerations, bent needles, and embedded needles have been reported when epinephrine injection has been injected into the thigh of young children who are uncooperative and kick or move during the injection [see *Warnings and Precautions (5.2)*].
- Injection into the buttock has resulted in cases of gas gangrene [see *Warnings and Precautions (5.2)*].

### Skin and Soft Tissue Infections

- Rare cases of serious skin and soft tissue infections, including necrotizing fasciitis and myonecrosis caused by Clostridia (gas gangrene), have been reported following epinephrine injection, including epinephrine injection 0.3 mg, in the thigh [see *Warnings and Precautions (5.3)*].

## 7 DRUG INTERACTIONS

### Cardiac Glycosides, Diuretics, and Anti-arrhythmics

Patients who receive epinephrine while concomitantly taking cardiac glycosides, diuretics, or anti-arrhythmics should be observed carefully for the development of cardiac arrhythmias [see *Warnings and Precautions (5.5)*].

### Antidepressants, Monoamine Oxidase Inhibitors, Levothyroxine, and Antihistamines

The effects of epinephrine may be potentiated by tricyclic antidepressants, monoamine oxidase inhibitors, levothyroxine sodium, and certain antihistamines, notably chlorpheniramine, tripelemamine, and diphenhydramine.

### Beta-Adrenergic Blockers

The cardiostimulating and bronchodilating effects of epinephrine are antagonized by beta-adrenergic blocking drugs, such as propranolol.

### Alpha-Adrenergic Blockers

The vasoconstricting and hypertensive effects of epinephrine are antagonized by alpha-adrenergic blocking drugs, such as phentolamine.

### Ergot Alkaloids

Ergot alkaloids may also reverse the pressor effects of epinephrine.

## 8 USE IN SPECIFIC POPULATIONS

### 8.1 Pregnancy

#### Risk Summary

There are no adequate and well controlled studies of the acute effect of epinephrine in pregnant women. In animal reproductive studies, epinephrine administered by the subcutaneous route to rabbits, mice, and hamsters during the period of organogenesis was teratogenic at doses 7 times and higher than the maximum recommended human intramuscular and subcutaneous dose on a mg/m<sup>2</sup> basis. Epinephrine is the first-line medication of choice for the treatment of anaphylaxis during pregnancy in humans. Epinephrine should be used for treatment of anaphylaxis during pregnancy in the same manner as it is used in non-pregnant patients. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

#### Clinical Considerations

##### Disease-associated maternal and embryo/fetal risk:

During pregnancy, anaphylaxis can be catastrophic and can lead to hypoxic-ischemic encephalopathy and permanent central nervous system damage or death in the mother and, more commonly, in the fetus or neonate. The prevalence of anaphylaxis occurring during pregnancy is reported to be approximately 3 cases per 100,000 deliveries.

Management of anaphylaxis during pregnancy is similar to management in the general population. Epinephrine is the first line-medication of choice for treatment of anaphylaxis; it should be used in the same manner in pregnant and non-pregnant patients. In conjunction with the administration of epinephrine, the patient should seek immediate medical or hospital care.

#### Data

##### Animal Data:

In an embryofetal development study with rabbits dosed during the period of organogenesis, epinephrine was shown to be teratogenic (including gastroschisis and embryonic lethality) at doses approximately 40 times the maximum recommended intramuscular or subcutaneous dose (on a mg/m<sup>2</sup> basis at a maternal subcutaneous dose of 1.2 mg/kg/day for two to three days).

In an embryofetal development study with mice dosed during the period of organogenesis, epinephrine was shown to be teratogenic (including embryonic lethality) at doses approximately 8 times the maximum recommended intramuscular or subcutaneous dose (on a mg/m<sup>2</sup> basis at maternal subcutaneous dose of 1 mg/kg/day for 10 days). These effects were not seen in mice at approximately 4 times the maximum recommended daily intramuscular or subcutaneous dose (on a mg/m<sup>2</sup> basis at a subcutaneous maternal dose of 0.5 mg/kg/day for 10 days).

In an embryofetal development study with hamsters dosed during the period of organogenesis from gestation days 7 to 10, epinephrine was shown to be teratogenic at doses approximately 7 times the maximum recommended intramuscular or subcutaneous dose (on a mg/m<sup>2</sup> basis at a maternal subcutaneous dose of 0.5 mg/kg/day).

### 8.2 Lactation

#### Risk Summary

There is no information on the presence of epinephrine in human milk, the effects on breastfed infants, or the effects on milk production. Epinephrine is the first line-medication of choice for treatment of anaphylaxis; it should be used in the same manner in breastfeeding and non-breastfeeding patients.

### 8.4 Pediatric Use

Epinephrine injection, 0.3 mg or epinephrine injection, 0.15 mg may be administered to pediatric patients at a dosage appropriate to body weight [see *Dosage and Administration (2.1)*]. Clinical experience with the use of epinephrine suggests that the adverse reactions seen in children

are similar in nature and extent to those both expected and reported in adults. Since the doses of epinephrine delivered from epinephrine injection, 0.3 mg and epinephrine injection, 0.15 mg are fixed, consider using other forms of injectable epinephrine if doses lower than 0.15 mg are deemed necessary.

### 8.5 Geriatric Use

Clinical studies for the treatment of anaphylaxis have not been performed in subjects aged 65 and over to determine whether they respond differently from younger subjects. However, other reported clinical experience with use of epinephrine for the treatment of anaphylaxis has identified that geriatric patients may be particularly sensitive to the effects of epinephrine. Therefore, epinephrine injection, 0.3 mg should be administered with caution in elderly individuals, who may be at greater risk for developing adverse reactions after epinephrine administration [see *Warnings and Precautions* (5.5), *Overdosage* (10)].

### 10 OVERDOSAGE

Overdosage of epinephrine may produce extremely elevated arterial pressure, which may result in cerebrovascular hemorrhage, particularly in elderly patients. Overdosage may also result in pulmonary edema because of peripheral vascular constriction together with cardiac stimulation. Treatment consists of rapidly acting vasodilators or alpha-adrenergic blocking drugs and/or respiratory support.

Epinephrine overdosage can also cause transient bradycardia followed by tachycardia, and these may be accompanied by potentially fatal cardiac arrhythmias. Premature ventricular contractions may appear within one minute after injection and may be followed by multifocal ventricular tachycardia (prefibrillation rhythm). Subsidence of the ventricular effects may be followed by atrial tachycardia and occasionally by atrioventricular block. Treatment of arrhythmias consists of administration of a beta-adrenergic blocking drug such as propranolol.

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

### 11 DESCRIPTION

Epinephrine Injection USP, 0.3 mg and Epinephrine Injection USP, 0.15 mg are single-dose auto-injectors and combination products containing drug and device components.

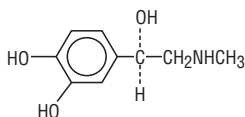
Each Epinephrine Injection USP, 0.3 mg (Auto-Injector) delivers a single dose of 0.3 mg epinephrine, USP from epinephrine injection USP, 0.3 mg/0.3 mL in a sterile solution.

Each Epinephrine Injection USP, 0.15 mg (Auto-Injector) delivers a single dose of 0.15 mg epinephrine, USP from epinephrine injection USP, 0.15 mg/0.3 mL in a sterile solution.

Each 0.3 mL in the Epinephrine Injection USP, 0.3 mg (Auto-Injector) contains 0.3 mg epinephrine USP, 1.8 mg sodium chloride, 0.4 mg sodium metabisulfite, 0.4 mg sodium tartrate (dihydrate), hydrochloric acid to adjust pH, and water for injection. The pH range is 2.2 to 5.0.

Each 0.3 mL in the Epinephrine Injection USP, 0.15 mg (Auto-Injector) contains 0.15 mg epinephrine USP, 1.8 mg sodium chloride, 0.4 mg sodium metabisulfite, 0.2 mg sodium tartrate (dihydrate), hydrochloric acid to adjust pH, and water for injection. The pH range is 2.2 to 5.0.

Epinephrine, USP is a sympathomimetic catecholamine. Chemically, epinephrine, USP is (-)-3,4-Dihydroxy- $\alpha$ -(methylamino)methylbenzyl 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, 0.3 mg and Epinephrine Injection USP, 0.15 mg if the epinephrine solution appears discolored (pinkish or darker than slightly yellow), cloudy, or if it contains a precipitate.

Thoroughly review the patient instructions and operation of Epinephrine Injection USP, 0.3 mg or Epinephrine Injection USP, 0.15 mg with patients and caregivers prior to use [see *Patient Counseling Information* (17)].

### 12 CLINICAL PHARMACOLOGY

#### 12.1 Mechanism of Action

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

#### 12.2 Pharmacodynamics

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

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

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

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

### 13 NONCLINICAL TOXICOLOGY

#### 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies to evaluate the carcinogenic potential of epinephrine have not been conducted. Epinephrine and other catecholamines have been shown to have mutagenic potential *in vitro*. Epinephrine was positive in the *Salmonella* bacterial reverse mutation assay, positive in the mouse lymphoma assay, and negative in the *in vivo* micronucleus assay. Epinephrine is an oxidative mutagen based on the *E. coli* WP2 Mutoxitest bacterial reverse mutation assay. This should not prevent the use of epinephrine where indicated [see *Indications and Usage* (1)].

The potential for epinephrine to impair reproductive performance has not been evaluated, but epinephrine has been shown to decrease implantation in female rabbits dosed subcutaneously with 1.2 mg/kg/day (40-fold the highest human intramuscular or subcutaneous daily dose) during gestation days 3 to 9.

### 16 HOW SUPPLIED/STORAGE AND HANDLING

#### How Supplied

Epinephrine Injection USP, 0.3 mg (Auto-Injectors) is supplied with two single-dose pre-filled auto-injectors and one auto-injector trainer device: 0.3 mg/0.3 mL (NDC 0093-5986-27).

Epinephrine Injection USP, 0.15 mg (Auto-Injectors) is supplied with two single-dose pre-filled auto-injectors and one auto-injector trainer device: 0.15 mg/0.3 mL (NDC 0093-5985-27).

Epinephrine Injection USP, 0.3 mg 2-Pack and Epinephrine Injection USP, 0.15 mg 2-Pack also includes a W-clip to clip two auto-injectors together.

#### Storage and Handling

- Protect from light. Epinephrine, USP is light sensitive and the auto-injector is manufactured from transparent UV stabilized polycarbonate to protect it from light.
- Store at 20° to 25°C (68° to 77°F); excursions permitted to 15° to 30°C (59° to 86°F) [See USP Controlled Room Temperature].
- Do not refrigerate.
- Before using, check to make sure the solution in the auto-injector is clear and colorless.
- Replace the auto-injector if the solution is discolored (pinkish or darker than slightly yellow), cloudy, or contains a precipitate.
- Properly dispose all used, unwanted or expired epinephrine injection, 0.3 mg and epinephrine injection, 0.15 mg auto-injectors.

KEEP THIS AND ALL MEDICATIONS OUT OF THE REACH OF CHILDREN.

### 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, 0.3 mg and epinephrine injection, 0.15 mg 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

Instruct patients and/or caregivers in the appropriate use of epinephrine injection, 0.3 mg and epinephrine injection, 0.15 mg should be injected into the middle of the outer thigh (through clothing, if necessary). Each device is a single-use injection. Advise patients to seek immediate medical care in conjunction with administration of epinephrine injection, 0.3 mg and epinephrine injection, 0.15 mg.

Instruct caregivers to hold the leg of young children firmly in place and limit movement prior to and during injection. Lacerations, bent needles, and embedded needles have been reported when epinephrine injection, 0.3 mg and epinephrine injection, 0.15 mg have been injected into the thigh of young children who are uncooperative and kick or move during an injection [see *Warnings and Precautions* (5.2)].

Instruct patients and/or caregivers to throw away the blue safety release immediately after using epinephrine injection, 0.3 mg and epinephrine injection, 0.15 mg. This small part may pose a choking hazard for children.

Complete patient information, including dosage, directions for proper administration and precautions can be found inside each epinephrine injection, 0.3 mg or epinephrine injection, 0.15 mg carton. A printed label on the surface of epinephrine injection, 0.3 mg and epinephrine injection, 0.15 mg shows instructions for use and a diagram depicting the injection process.

#### Training

Instruct patients and/or caregivers to use and practice with the Trainer to familiarize themselves with the use of epinephrine injection, 0.3 mg and epinephrine injection, 0.15 mg in an allergic emergency. The Trainer may be used multiple times. A Trainer device is provided in 2-Pack cartons.

Instruct patients and/or caregivers to immediately place the blue safety release back on the Trainer and reset it after practicing. This small part may pose a choking hazard for children.

#### Adverse Reactions

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

#### Accidental Injection

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

#### Serious Infections at the Injection Site

Rare cases of serious skin and soft tissue infections, including necrotizing fasciitis and myonecrosis caused by *Clostridia* (gas gangrene), have been reported at the injection site following epinephrine injection for anaphylaxis. Advise patients to seek medical care if they develop signs or symptoms of infection, such as persistent redness, warmth, swelling, or tenderness, at the epinephrine injection site [see *Warnings and Precautions* (5.3)].

#### Storage and Handling

Instruct patients to inspect the epinephrine solution visually through the clear window of the auto-injector periodically. Replace epinephrine injection, 0.3 mg and epinephrine injection, 0.15 mg if the epinephrine solution appears discolored (pinkish or darker than slightly yellow), cloudy or if it contains a precipitate. Epinephrine is light sensitive and should be protected from light. The auto-injector is not waterproof. Instruct patients that epinephrine injection, 0.3 mg and epinephrine injection, 0.15 mg must be used or properly disposed once the blue safety release is removed or after use [see *Storage and Handling* (16.2)].

Advise patients and caregivers to give used epinephrine injection, 0.3 mg and epinephrine injection, 0.15 mg auto-injectors to their healthcare provider for inspection and proper disposal. Advise patients and caregivers to promptly dispose of medicines that are no longer needed. Dispose of expired, unwanted, or unused epinephrine injection, 0.3 mg and epinephrine injection, 0.15 mg auto-injectors in an FDA-cleared sharps container. Instruct patients not to dispose epinephrine injection, 0.3 mg or epinephrine injection, 0.15 mg in their household trash. Instruct patients that if they do not have a FDA-cleared sharps disposal container, they may use a household container that is made of a heavy-duty plastic, can be closed with a tight-fitting and puncture-resistant lid without sharps being able to come out, upright and stable during use, leak-resistant, and properly labeled to warn of hazardous waste inside the container. Inform patients that they can visit the FDA website for additional information on disposal of unused medicines.

Complete patient information, including dosage, directions for proper administration and precautions can be found inside each epinephrine injection, 0.3 mg (Auto-Injector) and epinephrine injection, 0.15 mg (Auto-Injector) carton.

Manufactured For:

**Teva Pharmaceuticals USA, Inc.**

North Wales, PA 19454

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The Teva logo consists of the word "teva" in a bold, lowercase, sans-serif font. The letter 'v' is stylized with a diagonal slash through it.

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