PRESCRIBING INFORMATION

Twinject® 0.3 mg Auto-Injector
Epinephrine Injection, USP

Twinject® 0.15 mg Auto-Injector
Epinephrine Injection, USP

Amedra Pharmaceuticals LLC
Horsham, PA
19044 USA

Distributed by:
Paladin Labs Inc.
Montreal, QC
H4P 2T4

Date of Revision:
December 12, 2012

Control No. 158595

TABLE OF CONTENTS

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Product	Dosage Form / Strength	Clinically Relevant Non Medicinal Ingredients
Injection	Twinject 0.3 mg Auto-Injector	Syringe, 1:1000 2 doses 0.3 mg each	*For a complete listing see* ***DOSAGE FORMS, COMPOSITION AND PACKAGING*** *section.*
	Twinject 0.15 mg Auto-Injector	Syringe, 1:1000 2 doses 0.15 mg each	

INDICATIONS AND CLINICAL USE

Epinephrine is the drug of choice for the emergency treatment of severe allergic reactions (Type I) to allergens, such as those present in certain insect venoms, foods, latex, or drugs.

Twinject® 0.3 mg Auto-Injector (Epinephrine Injection, USP) and Twinject® 0.15 mg Auto-Injector (Epinephrine Injection, USP) are indicated for the emergency treatment of severe allergic reactions (Type 1) 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 (peanuts, tree nuts, such as walnuts, hazelnuts, almonds, cashews, pecans, pistachios, shellfish, fish, milk, eggs and wheat).
- latex,
- other allergens,
- drugs.

Epinephrine can also be used in the treatment of anaphylaxis of unknown cause (idiopathic anaphylaxis), exercise-induced anaphylaxis (anaphylaxis occurring when exercise takes place within 2 to 4 hours of ingesting a specific food such as celery, shellfish, or wheat), or anaphylactoid reactions (these reactions are clinically indistinguishable from anaphylaxis, but are not IgE mediated and are seen in response to opiates, NSAIDs and radiocontrast agents).

The Canadian Pediatric Surveillance Program defines anaphylaxis as “a severe allergic reaction to any stimulus, having sudden onset and generally lasting less than 24 hours, involving one or more body systems and producing one or more symptoms such as hives, flushing, itching, angioedema, stridor, wheezing, shortness of breath, vomiting, diarrhea, or shock.” Because anaphylaxis is a generalized reaction, a wide variety of clinical signs and symptoms may be observed.

In the general population, 1% to 2% is estimated to be at risk for anaphylaxis from food allergies and insect stings, with a lower reported prevalence for drugs and latex. Asthmatic subjects are at particular risk.

Clinical Signs and Symptoms of Anaphylaxis
(Sampson HA. Anaphylaxis and emergency treatment. *Pediatrics*. 2003 Jun: 111(6 Pt3): 1601-8)

Oral: pruritus of lips, tongue, and palate and edema of lips and tongue; metallic taste in the mouth

Cutaneous: flushing, pruritus, urticaria, angioedema, morbilliform rash, and pilor erecti

Gastrointestinal: nausea, abdominal pain (colic), vomiting (large amounts of "stringy" mucus), and diarrhea

Respiratory (major shock organ): laryngeal: pruritus and "tightness" in the throat, dysphagia, dysphonia and hoarseness, dry "staccato" cough, and sensation of itching in the external auditory canals, "deep" cough, and wheezing; nose pruritus, congestion, rhinorrhea, and sneezing

Cardiovascular: feeling of faintness, syncope, chest pain, dysrhythmia, hypotension

Other: periorbital pruritus, erythema and edema, conjunctival erythema, and tearing; lower back pain and uterine contractions in women; aura of "doom"

Hypotension is a **late** sign of anaphylaxis. Patients should be treated in the early stages of anaphylaxis in order to **prevent** hypotension from developing.

The severity of previous anaphylactic reactions does not determine the severity of future reactions, and subsequent reactions could be the same, better, or worse. The unpredictability depends on the degree of allergy and the dose of allergen.

Epinephrine should be administered as early as possible after the onset of symptoms of severe allergic response. Patients requiring epinephrine will not always have predictable reactions. Adequate warning signs are not always present before serious reactions occur.

It is recommended that epinephrine be given at the start of any reaction occurring in conjunction with a known or suspected allergy contact. In patients with a history of a severe cardiovascular collapse to an allergen the physician may advocate that epinephrine be administered immediately after an insect sting or ingestion of the offending food and before any reaction has begun.

Epinephrine, when used as directed immediately following exposure to an allergen, may prove life-saving.

More than 2 sequential doses of epinephrine should only be administered under direct medical supervision.

Under physician-supervised care, epinephrine can be re-injected every 5 to15 minutes until there is resolution of the anaphylaxis or signs of hyperadrenalism occur (including palpitations, tremor, uncomfortable apprehension and anxiety).

Epinephrine in the majority of cases will be effective after one injection. However, **all** patients receiving emergency epinephrine must immediately be transported to an emergency medical facility. Further treatments may be required and therefore observation in an emergency medical setting is necessary. It is strongly recommended that patients (including individuals with milder reactions) should be observed for 4 hours after initial symptoms of anaphylaxis subside.

Anaphylactic reactions typically follow a uniphasic course; however, 20% will be biphasic in nature. The second phase usually occurs after an asymptomatic period of 1 to 8 hours, but may occur up to 38 hours (mean 10 hours) after the initial reaction. About one-third of the second-phase reactions are more severe, one-third are as severe and one-third are less severe. The second-phase reactions can occur even following administration of corticosteroids. It is recommended that following successful treatment of anaphylaxis, the patient should stay where he or she can call 911 with timely delivery to hospital for the next 48 hours.

Protracted anaphylaxis, which is frequently associated with profound hypotension and sometimes lasts longer than 24 hours, is minimally responsive to aggressive therapy, and has a poor prognosis.

Epinephrine injections are designed as emergency supportive therapy only and are not a replacement or substitute for immediate medical care.

CONTRAINDICATIONS

There are no known contraindications to the use of epinephrine in a life-threatening allergic reaction.

WARNINGS AND PRECAUTIONS

General

Patients with a history of anaphylaxis are at risk for subsequent episodes and death. All patients who have had one or more episodes of anaphylaxis should have injectable epinephrine with them or with their parent or caregiver at all times, and should wear some form of medical identification bracelet or necklace.

Epinephrine Injection, USP is not intended as a substitute for medical attention or hospital care. In conjunction with the administration of epinephrine, the patient should seek appropriate medical care.

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

Twinject® 0.3 mg Auto-Injector and Twinject® 0.15 mg Auto-Injector should only be injected into the anterolateral aspect of the thigh (mid outer thigh). Accidental injection into the hands or feet may result in loss of blood flow to the affected area and should be avoided.

Avoid possible inadvertent intravascular administration.

Do not inject intravenously. The marked pressor effects may be counteracted by use of rapidly acting vasodilators.

Larger doses or accidental intravenous administration may induce severe hypertension, or cerebrovascular hemorrhage due to a sharp rise in blood pressure.

It should be determined whether the patient is at risk for future anaphylaxis, since there are some concerns in specific patients with epinephrine administration. Despite these concerns, epinephrine is essential for the treatment of anaphylaxis.

The presence of these conditions is not a contraindication to epinephrine administration in an acute, life-threatening situation. Therefore, patients with these conditions, or any other person who might be in a position to administer epinephrine to a patient with these conditions experiencing anaphylaxis, should be instructed about the circumstances under which epinephrine should be used.

Carcinogenesis and Mutagenesis
There are no data from either animal or human studies regarding the carcinogenicity or mutagenicity of epinephrine.

Cardiovascular
Epinephrine use should be avoided in patients with cardiogenic, traumatic, or hemorrhagic shock; cardiac dilation; and/or cerebral arteriosclerosis.

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

In patients with coronary insufficiency or ischemic heart disease, epinephrine may precipitate or aggravate angina pectoris as well as produce potentially fatal ventricular arrhythmias.

Patients with hypertension or hyperthyroidism are prone to more severe or persistent effects, as are patients with coronary artery disease, who may experience angina.

Endocrine and Metabolism
Patients with diabetes may develop increased blood glucose levels following epinephrine administration.

Neurologic
Epinephrine use should be avoided in patients with organic brain damage.

Patients with Parkinson's disease may notice a temporary worsening of symptoms after treatment with epinephrine.

Ophthalmologic
Epinephrine use should be avoided in patients with narrow-angle glaucoma.

Respiratory
Studies have shown a significant increased risk of near fatal and fatal reactions in patients with coexistent asthma.

Fatalities may also occur from pulmonary edema resulting from peripheral constriction and cardiac stimulation.

Sensitivity
Epinephrine is the preferred treatment for serious allergic 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 presence of sulfite(s) in this product should not deter administration of the drug for treatment of serious allergic or other emergency situations, even if the patient is sulfite-sensitive.

Reproduction
No studies have been conducted to determine epinephrine's potential for the impairment of fertility.

Special Populations
Geriatrics (> 65 years of age):
Elderly patients with hypertension, arteriopathies or known ischaemic heart disease are particularly at risk for epinephrine overdose. Careful monitoring and avoidance of epinephrine overdose is necessary in these patients.

Pediatrics (patients 33-65 pounds or 15-30 kg):
There are no data to suggest a difference in safety or effectiveness of epinephrine between adults and children.

See **DOSAGE AND ADMINISTRATION** section for dosage requirements based on weight.

Pregnancy:
Teratogenic Effects. Pregnancy Category C – Epinephrine has been shown to have developmental effects in rabbits at a subcutaneous dose of 1.2 mg/kg (approximately 30 times the maximum recommended daily subcutaneous or intramuscular dose on a mg/m^2 basis), in

mice at a subcutaneous dose of 1 mg/kg (approximately 7 times the maximum recommended daily subcutaneous or intramuscular dose on a mg/m^2 basis), and in hamsters at a subcutaneous dose of 0.5 mg/kg (approximately 5 times the maximum recommended daily subcutaneous or intramuscular dose on a mg/m^2 basis).

These effects were not seen in mice at a subcutaneous dose of 0.5 mg/kg (approximately 3 times the maximum recommended daily subcutaneous or intramuscular dose on a mg/m^2 basis).

Although there are no adequate and well-controlled studies in pregnant women, epinephrine crosses the placenta and could lead to fetal anoxia, spontaneous abortion or both.

Epinephrine Injection, USP (1:1000) should be used in pregnancy only if the potential benefit justifies the potential risk to the fetus.

ADVERSE REACTIONS

Adverse Drug Reaction Overview

Adverse reactions include transient, moderate anxiety; feelings of over stimulation; apprehensiveness; restlessness; tremor; weakness; shakiness; dizziness; sweating; an increase in pulse rate; the sensation of a more forceful heartbeat; palpitations; pallor; nausea and vomiting; headache, and/or respiratory difficulties.

While these symptoms occur in some patients treated with epinephrine, they are more likely to be pronounced in patients with hypertension or hypothyroidism.

These signs and symptoms usually subside rapidly, especially with rest, quiet, and recumbency.

Some patients may be at greater risk of developing adverse reactions after epinephrine administration. These include elderly individuals, pregnant women, and patients with diabetes.

Patients with coronary artery disease are prone to more severe or persistent effects, and may experience angina.

Excessive doses cause acute hypertension. Rapid rises in blood pressure have produced cerebral hemorrhage, particularly in elderly patients with cardiovascular disease.

Arrhythmias, including fatal ventricular fibrillation, have been reported, particularly in patients with underlying cardiac disease or those receiving certain drugs (see “Drug Interactions”).

The potential for epinephrine to produce these types of adverse reactions does not contraindicate its use in an acute life-threatening allergic reaction.

DRUG INTERACTIONS

Overview
There are no known contraindications to the use of epinephrine in a life-threatening allergic reaction.

Drug-Drug Interactions
Epinephrine should be used with caution in patients who are on medications that may sensitize the heart to arrhythmias, e.g., digitalis, diuretics, or anti-arrhythmics. In such patients, epinephrine may precipitate or aggravate angina pectoris as well as produce ventricular arrhythmias.

Caution is indicated in patients receiving cardiac glycosides or mercurial diuretics, since these agents may sensitize the myocardium to beta-adrenergic stimulation and make cardiac arrhythmias more likely.

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

The cardiostimulating and bronchodilating effects of epinephrine are antagonized by beta-adrenergic blocking drugs, such as propranolol. Anaphylaxis may be made worse by beta blockers, and these drugs decrease the effectiveness of epinephrine.

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

Ergot alkaloids and phenothiazines may also reverse the pressor effects of epinephrine.

Deaths have been reported in asthmatics treated with epinephrine following the use of isoproterenol or orciprenaline.

Drug-Food Interactions
Interactions with food have not been established.

Drug-Herb Interactions
Interactions with herbal products have not been established.

Drug-Laboratory Interactions
Interactions with laboratory tests have not been established.

Drug-Lifestyle Interactions
Cocaine sensitizes the heart to catecholamines (as does uncontrolled hyperthyroidism), and epinephrine use in these patients should be administered cautiously.

DOSAGE AND ADMINISTRATION

Dosing Considerations

The prescribing physician 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 being prescribed.

Since the dose of epinephrine delivered from Twinject® 0.15 mg is fixed at 0.15 mg, the physician should consider other forms of injectable epinephrine if doses lower than 0.15 mg are felt to be necessary (e.g. for children weighing less than 15 kilograms [approximately 33 pounds]).

The second dose should be injected in approximately 10 minutes if symptoms worsen or if there is no clinical improvement, and if the patient has not yet reached an emergency medical facility for treatment.

More than 2 sequential doses of epinephrine should only be administered under direct medical supervision.

Recommended Dose and Dosage Adjustment

Twinject® 0.3 mg Auto-Injector

This product is intended for use by adults and children who weigh 30 kilograms (approximately 66 pounds) or more only.

Twinject 0.3 mg is capable of delivering two doses of 0.3 mg (0.3 mL of 1:1000 dilution of epinephrine) each.

The first dose is available for auto-injection by the patient. With persistent symptoms of anaphylaxis, a second dose is available for manual injection by the patient following a partial disassembly of the Twinject® 0.3 mg Auto-Injector.

Twinject® 0.15 mg Auto-Injector

This product is intended for use by adults and children who weigh 15 to 30 kilograms (approximately 33 to 66 pounds).

Twinject 0.15 mg is capable of delivering two doses of 0.15 mg (0.15 mL of 1:1000 dilution of epinephrine) each.

The first dose is available for auto-injection by the patient or caregiver. With persistent symptoms of anaphylaxis, a second dose is available for manual injection by the patient or caregiver following a partial disassembly of the Twinject® 0.15 mg Auto-Injector.

A dosage of 0.01 mg/kg body weight is usually recommended for pediatric patients.

Administration

Patients with a history of severe allergic reactions should be instructed about the circumstances under which epinephrine should be used (See **INDICATIONS AND CLINICAL USE** Section).

The patient's physician or pharmacist should review the package insert in detail with the patient or caregiver to insure that he/she understands the indications and use of Twinject 0.3 mg or Twinject 0.15 mg Auto-Injector.

Actual demonstration of the injection technique by a physician or a pharmacist is recommended. A demonstrator unit which does not contain a needle or epinephrine is available for this purpose.

Product is intended for subcutaneous or intramuscular use. Do not inject into buttock.

The first dose is delivered automatically after the patient prepares the Twinject 0.3 mg Auto-Injector or Twinject 0.15 mg Auto-Injector for firing as directed.

Inject the delivered dose of the Twinject 0.3 mg Auto-Injector (0.3 mL epinephrine injection, USP, 1:1000) or the Twinject 0.15 mg Auto-Injector (0.15 mL epinephrine 1:1000) subcutaneously or intramuscularly into the anterolateral (mid outer thigh) aspect of the thigh, through clothing if necessary.

A second, manually administered dose is available following a partial disassembly of the Twinject 0.3 mg or Twinject 0.15 mg Auto-Injector.

If the second dose is not needed, discard Twinject (including unused epinephrine) as directed at the end of this package insert or in the instructions inside each Twinject 0.3 mg and Twinject 0.15 mg package.

OVERDOSAGE

Epinephrine is rapidly inactivated in the body, and treatment following overdose with epinephrine is primarily supportive. If necessary, pressor effects may be counteracted by rapidly acting vasodilators or alpha-adrenergic blocking drugs.

If prolonged hypotension follows such measures, it may be necessary to administer another pressor drug.

Overdosage of epinephrine may produce extremely elevated arterial pressure, which may result in cerebrovascular hemorrhage, particularly in elderly patients.

If an epinephrine overdose induces pulmonary edema that interferes with respiration, treatment consists of a rapidly acting alpha-adrenergic blocking drug and/or intermittent positive-pressure respiration.

Epinephrine overdosage can also cause transient bradycardia followed by tachycardia, and these may be accompanied by potentially fatal cardiac arrhythmias. Treatment of arrhythmias consists of administration of a beta-adrenergic blocking drug such as propranolol.

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.

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

STORAGE AND STABILITY

Patients should be instructed to periodically check the expiration date and visually inspect the epinephrine solution for particulate matter and discolouration.

Epinephrine deteriorates rapidly on exposure to air or light, turning pink from oxidation to adrenochrome and brown from the formation of melanin.

If the solution contains particulate matter or develops a pinkish colour or becomes darker than slightly yellow, the patient should immediately contact their physician or pharmacist for a replacement, since these changes indicate that the effectiveness of the drug product might have decreased. Epinephrine solutions that show evidence of discolouration should be discarded.

Epinephrine is light sensitive and should be stored in the case provided. Protect from light.

Store at 20-25°C (with excursions permitted to 15-30°C). Protect from freezing. Do not refrigerate.

Keep out of reach of children.

DOSAGE FORMS, COMPOSITION AND PACKAGING

The Twinject® 0.3 mg or Twinject® 0.15 mg Auto-Injector unit is designed to be compact and easy to carry, and to provide emergency treatment when medical care is not immediately available.

Highly sensitive individuals should have epinephrine injectable products readily available at all times.

Twinject® 0.3 mg Auto-Injector
A patient-actuated single-use auto-injection device that contains 1.1 mL Epinephrine Injection, USP in a sterile syringe designed to deliver 2 doses of 0.3 mL each.

Once fired, the Twinject® 0.3 mg will administer one 0.3 mL (0.3 mg) dose. A second 0.3 mL dose of epinephrine is available by manual administration. There is residual epinephrine left in the syringe following delivery of the second dose.

Each 0.3 mL dose contains 1.5 mg chlorobutanol, 0.3 mg *l*-epinephrine, 0.45 mg sodium bisulfite, 2.6 mg sodium chloride and water for injection. Sealed under nitrogen.

Twinject® 0.3 mg Auto-Injector is available in a single unit carton; it is also available in a Twinpack format, containing two Twinject Auto-Injectors and one demonstrator.

Twinject® 0.15 mg Auto-Injector
A patient-actuated single-use auto-injection device that contains 1.1 mL Epinephrine Injection, USP in a sterile syringe designed to deliver 2 doses of 0.15 mL each.

Once fired, the Twinject® 0.15 mg will administer one 0.15 mL (0.15 mg) dose. A second 0.15 mL dose of epinephrine is available by manual administration. There is residual epinephrine left in the syringe following delivery of the second dose.

Each 0.15 mL dose contains 0.75 mg chlorobutanol, 0.15 mg *l*-epinephrine, 0.225 mg sodium bisulfite,1.3 mg sodium chloride and water for injection. Sealed under nitrogen.

Twinject® 0.15 mg Auto-Injector is available in a single unit carton; it is also available in a Twinpack format, containing two Twinject Auto-Injectors and one demonstrator.

PART II: SCIENTIFIC INFORMATION

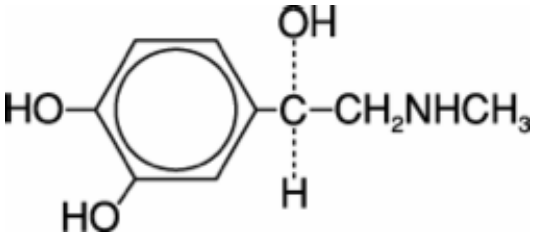
PHARMACEUTICAL INFORMATION

DRUG SUBSTANCE

Proper name: Epinephrine

Chemical name: 1-(3,4-dihydroxyphenyl)-2-(methylamino)ethanol

Structural formula:



Physicochemical properties: Epinephrine is a sympathomimetic catecholamine. Its naturally occurring *l*-isomer, which is twenty times as active as the *d*-isomer, is obtained in pure form by separation from the synthetically produced racemate.

ACTION OF DRUG SUBSTANCE

Epinephrine acts on both alpha and beta adrenergic receptors.

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

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

Epinephrine also helps to alleviate pruritus, urticaria, and angioedema, and may be effective in relieving gastrointestinal and genitourinary symptoms of anaphylaxis because of its relaxer effects on the smooth muscle of the stomach, intestine, uterus and urinary bladder.

Epinephrine, when given intramuscularly or subcutaneously, has a rapid onset and short duration of action.

Epinephrine Injection, USP Manufactured by Hospira, Inc., Lake Forest, IL 60045 USA

IMPORTANT: PLEASE READ

PART III: CONSUMER INFORMATION

TWINJECT®
(Epinephrine Injection, USP)

This leaflet is part III of a three-part "Prescribing Information" published when Twinject® was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not provide you all the information about Twinject®. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What is Twinject® used for?
Your doctor has prescribed Twinject® for the emergency treatment of severe allergic reactions including anaphylaxis.

What is anaphylaxis?
Anaphylaxis is a severe allergic reaction that may affect your whole body. It occurs soon after exposure to a specific allergen (the substance you are allergic to). Anaphylaxis can result in death and thus requires immediate attention and treatment. It may subside quickly with treatment or it may last 2-3 hours. It may also reoccur after you feel better, occasionally up to 24 hours later.

What are the common causes of anaphylaxis?
Any substance has the potential to cause anaphylaxis, but the most common causes are insect stings (particularly wasps), foods (especially peanuts, tree nuts, shellfish and fish, milk and eggs), medications (particularly penicillin and other antibiotics) and latex. Exercise can produce anaphylaxis, and sometimes no obvious cause can be determined.

What are the symptoms of an anaphylaxis?
After contact with any of the above substances, symptoms may occur suddenly or come on gradually. Typically, one or more of the listed symptoms may occur and usually follow the same pattern each time, although the degree of severity may change:

- Itching/hives
- Difficulty breathing or swallowing
- Wheezing
- Flushing
- Swelling of your lips, tongue, face or throat
- Abdominal pain and vomiting
- Palpitation (the sensation of your heart beating fast)
- Dizziness/light-headedness
- Any feelings/symptoms that you experienced with your last reaction.
- Decreased blood pressure
- Paleness
- Weakness
- Anxiety
- Collapse or loss of consciousness

What does Twinject® do?
Epinephrine is a rapid-onset, short-acting medication that helps to decrease your body's allergic reaction. Some of the ways it works include:

- relaxing the muscles in your airways so you can breathe more easily;
- helping to reverse the rapid and dangerous decrease in blood pressure;
- relaxing the muscles in your gastrointestinal and genitourinary systems (e.g., stomach, intestines, uterus and bladder); and
- relieving allergy-caused swelling, itching and rash.

What dosage forms Twinject® comes in:
Twinject is a prefilled auto-injection device containing epinephrine solution. The auto-injector unit is designed to be compact and easy to carry and to provide emergency treatment when medical care is not immediately available. Please see the **PATIENT DIRECTIONS** section for more information on the auto-injector at the end of this Prescribing Information.

Twinject® is available in two (2) dosing strengths. Twinject® 0.15 mg is for those who weigh between 15 and 30 kilograms (about 33 to 66 pounds). Twinject® 0.3 mg is for those who weigh 30 kilograms (about 66 pounds) or more.

Each strength of Twinject is also available in a Twinpack format, containing two Twinject Auto-Injectors and one demonstrator.

What the medicinal ingredient is:

Each 0.3 mL dose contains 0.3 mg epinephrine. Each 0.15 mL dose contains 0.15 mg epinephrine.

What the important nonmedicinal ingredients are:

Each 0.3 mL dose contains 1.5 mg chlorobutanol, 0.45 mg sodium bisulfite, 2.6 mg sodium chloride and water for injection. Sealed under nitrogen.

Each 0.15 mL dose contains 0.75 mg chlorobutanol, 0.225 mg sodium bisulfite,1.3 mg sodium chloride and water for injection. Sealed under nitrogen.

WARNINGS AND PRECAUTIONS

Remember, this medicine is prescribed for the particular condition that you have. Do not give this medicine to other people, nor use it for any other condition. Read the following information carefully. If you need any explanations, or further information, ask your physician or pharmacist.

BEFORE you use Twinject®, talk to your doctor or pharmacist if you:

- have or have had heart disease, irregular heart beat or high blood pressure,
- are pregnant or may become pregnant,
- have diabetes,
- have thyroid conditions,
- have narrow-angle glaucoma,
- have depression or mental illness,
- are allergic to any of the ingredients,
- have asthma,
- have previously had an allergic reaction, or
- have Parkinson's disease.

Tell your doctor about all of your medical problems or conditions such as a serious injury, a serious infection or major surgery.

INTERACTIONS WITH THIS MEDICATION

Before your treatment with Twinject®, tell your doctor about all the medicines you take, including prescription and non-prescription drugs, vitamins and herbal remedies.

Twinject® should be used with caution if you are taking

- Alpha-adrenergic blocking drugs, such as phentolamine;
- Antihistamines, such as chlorpheniramine, tripelennamine, or diphenhydramine (these can be available over-the-counter);
- Beta-adrenergic blocking drugs, such as propranolol;
- Cocaine;
- Diuretic medicines ("water pills");
- Ergot alkaloids and phenothiazines;
- Heart rhythm medicine, such as digoxin or quinidine (another name for digoxin is digitalis);
- Isoproterenol or orciprenaline (for asthma);
- MAO inhibitors (MAOI), such as selegilline, isocarboxazid, phenelzine sulphate, or tranylcypromine;
- Thyroid medications (e.g., sodium levothyroxine); or
- Tricyclic antidepressants, such as amitriptyline, doxepin, nortriptyline.

PROPER USE OF THIS MEDICATION

IMPORTANT NOTE: Anaphylaxis can result in death if not properly treated. If you experience any symptoms of anaphylaxis mentioned in the ABOUT THIS MEDICATION section, you should administer Twinject® immediately, then contact your doctor afterwards.

Usual Dose:

Twinject® should be used **immediately** after you notice the symptoms of anaphylaxis.

Twinject® 0.3 mg should be used for adults and children weighing 30 kg or more. A second 0.3 mL dose is available by manual administration **to be used if the symptoms persist.**

Twinject 0.15 mg should be used for children weighing between 15-30 kg. A second 0.15 mL dose is available by manual administration **to be used if the symptoms persist.**

Some medication will be left over in the syringe after delivery of the second dose.

For children weighing less than 15 kg (almost 33 pounds), please talk to your doctor or pharmacist.

Even if you respond to Twinject®, you should seek medical attention immediately, because you may

need further treatment and monitoring. Sometimes the epinephrine may make you feel anxious or as if your heart is racing - this is a normal side effect of the medication.

Even after you feel better, there is a possibility that some or all of your anaphylactic symptoms could reoccur. This will usually happen in the first 10 hours after you get better, but could be anytime from a few minutes to 24 hours after the first reaction. Thus, it is essential that you remain within close access of a hospital or the emergency response system (i.e., 911).

Medical identification bracelets or wallet cards are also recommended to help communicate information about your serious allergies to caregivers and medical personnel.

Checklist:

- ❑ Diagnosis of allergies by a physician or an allergist.
- ❑ Identify the allergens or triggers by a physician or an allergist.
- ❑ Discuss treatment plan with a physician or an allergist.
- ❑ Develop a strategy to avoid your allergens or triggers.
- ❑ Create a list of the signs and symptoms associated with your particular anaphylaxis.
- ❑ Train in the use of Twinject® from a physician or a pharmacist.
- ❑ Carry your Twinject® with you at all times.
- ❑ Check the expiry date of Twinject® monthly and replace the outdated injection promptly.
- ❑ Carry medical identification bracelet or wallet cards to help communicate information about your serious allergies.
- ❑ Obtain educational material from the Anaphylaxis Project of the Allergy Asthma Information Association.

PATIENT DIRECTIONS

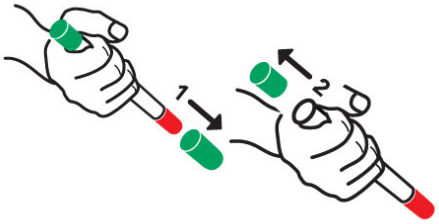
Make Sure That The Medicine Is Ready

Examine Twinject® 0.3 mg or Twinject® 0.15 mg regularly. It may not work if the medicine looks cloudy (has particles), pinkish or more than slightly yellow, or if the expiration date has passed.

Do **NOT** remove **GREEN** caps until you are ready to use Twinject®.

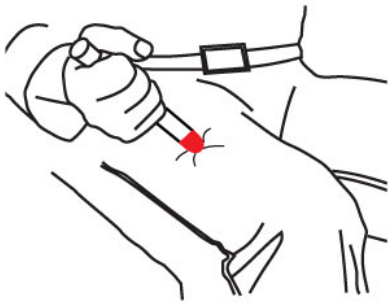
FIRST DOSE
STEP A
Important: follow these steps in the correct order

- Pull off **GREEN** end cap marked [1] first; you will now see a red tip. Never put thumb, finger or hand over the **RED** tip**.**
- Next, pull off **GREEN** cap marked [2].



STEP B

- Put the **RED** tip against middle of the outer side of your thigh (upper leg) as shown. It can go through clothes.
- Press down hard until the needle enters your thigh (upper leg) through your skin. Hold it in place while slowly counting to 10 to make sure that all medicine is delievered.



- Remove Twinject® from your thigh.
- Check the **RED** tip; if the needle is exposed, you received the dose. If needle is not visible, repeat First Dose, Step B.
- **Get emergency medical help right away; stay where you can call 911 or within easy access of a hospital for the next 48 hours.**
- **Immediately prepare for second dose.**

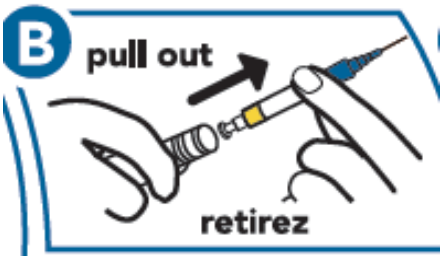
It is very important to monitor symptoms closely after the first dose is given including watching for new symptoms. If new symptoms have appeared or symptoms have not improved within 10 minutes, a second dose is needed.

SECOND DOSE
STEP A

- Unscrew and remove **RED** tip.
  Be careful of exposed needle.

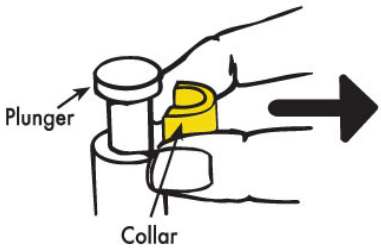
STEP B

- Grab the **BLUE** plastic to pull the syringe out of the barrel (do not touch the needle).



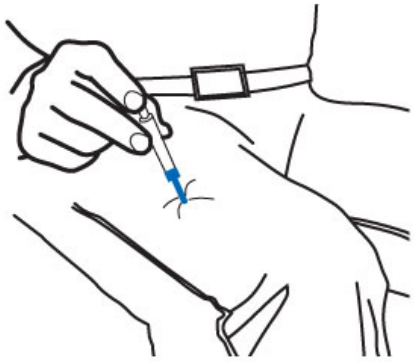
STEP C

- Slide the **YELLOW** collar off the plunger. Be careful not to pull up on the plunger while removing the **YELLOW** collar.



STEP D

- If your symptoms have not improved within 10 minutes since the first injection, you need a second dose.
- Put the needle into your thigh (upper leg), through your skin as shown.
- Push plunger down all the way until it cannot go any further.



- Remove Twinject® from your skin.
- Get emergency medical help right away.
- If a second dose is not needed and after professional medical attention is received, throw away the unused medicine as directed in syringe disposal directions of this leaflet.
- After the first and second dose, liquid will remain in the syringe that can't be used.

SYRINGE DISPOSAL:

- Put the syringe, needle first, into the carrying case.
- Put the other half of the carrying case on and close it.
- Give your used Twinject® to a healthcare worker for proper disposal. **Do not throw away in trash.**

Overdose:

In case of drug overdose, contact a health care practitioner, hospital emergency department, or regional Poison Control Centre immediately, even if there are no symptoms.
Too much epinephrine can cause dangerously high blood pressure, stroke, or death. If you take more than the recommended dose, or inject the Auto-Injector anywhere other than your thigh, make sure that you speak to your doctor or pharmacist immediately.

SIDE EFFECTS AND WHAT TO DO ABOUT

Twinject® may cause temporary, moderate anxiety; feelings of over-stimulation; apprehensiveness; restlessness; tremor; weakness; shakiness; dizziness; sweating; an increase in pulse rate; the sensation of a more forceful heartbeat; paleness; nausea and vomiting; headache; and/or breathing difficulties. These signs and symptoms usually go away quickly, especially with rest, quiet and lying down.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
    - Fax toll-free to 1-866-678-6789, or
    - Mail to :
      Canada Vigilance Program
      Health Canada
      Postal Locator 0701E
      Ottawa, ON K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

Note: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

HOW TO STORE THIS MEDICATION

Store Twinject® in the provided carrying case at room temperature (20-25°C/68-77°F) with excursions permitted to 15-30°C (59-86°F). Protect from freezing. Do not refrigerate. Protect from light.

Keep in a safe place out of reach of children.

Periodically, inspect your Twinject® unit and **do not use** if it looks cloudy (has particles), is pinkish or more than slightly yellow or if the expiration date has passed. If any of these changes have occurred contact your doctor or pharmacist for a replacement.

MORE INFORMATION

This document plus the full product monograph prepared for health professionals can be obtained by contacting:

By mail:
Paladin Labs Inc.
6111 Royalmount Ave., Suite 102
Montreal, QC H4P 2T4

By telephone: 1-888-550-6060

This leaflet was prepared by Paladin Labs Inc.
Last revised: November 2012

Manufactured for:
Amedra Pharmaceuticals LLC
Horsham, PA
USA

Distributed by:
Paladin Labs Inc.
Montreal, QC H4P 2T4
1-888-550-6060

Epinephrine Injection, USP (1:1000) manufactured by Hospira, Inc. Lake Forest, IL 60045 USA

This product may be covered by some or all of the following patents, patent application, and foreign equivalents thereof: CA Patent 2163005, US Patent Nos. 5,358,489; 5,540,664; 5,665,071; and 7,297,136 and other pending US and international applications.

Revision: December 12, 2012