Self-Injectable Epinephrine Agents

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Self-Injectable Epinephrine Agents

FDA Approved Indications[1,2,3]

Drug	Manufacturer	FDA-Approved Indications
epinephrine 0.3 mg (Adrenaclick® 0.3 mg)	Sciele	♦ Emergency treatment of Type I allergic reactions including anaphylaxis to stinging insects, biting insects, allergen immunotherapy, foods, drugs, diagnostic testing substances, and other allergens ♦ Emergency treatment of idiopathic anaphylaxis ♦ Emergency treatment of exercise-induced anaphylaxis
epinephrine 0.15 mg (Adrenaclick® 0.15 mg)	Sciele	
epinephrine 0.3 mg (Epi Pen®)	Meridian/Dey	
epinephrine 0.15 mg (Epi Pen® Jr.)	Meridian/Dey	
epinephrine 0.3 mg (Twinject®)	Sciele	
epinephrine 0.15 mg (Twinject® Jr.)	Sciele	

Overview

Anaphylaxis is an acute, life-threatening medical emergency with many potential triggers. A severe systemic allergic reaction is potentially fatal.[4] The condition requires prompt recognition and immediate management. Anaphylaxis has a rapid onset with multiple organ-system involvement and is mostly caused by specific antigens in sensitized individuals. Reactions typically follow a uniphasic pattern, however, about 20 percent will be biphasic in nature. The second phase usually occurs after an asymptomatic period of one to eight hours with as much as a 24 hour delay. Protracted anaphylaxis may persist beyond 24 hours. Concurrent beta-blocker therapy may adversely affect the response to management. Epinephrine is the treatment of choice and should be administered immediately. Secondary measures include circulatory support, antihistamines (both H_1 and H_2 antagonists), corticosteroids and, occasionally, bronchodilators. Careful post-treatment observation of patients who suffer an anaphylactic episode is necessary with ready access to emergency care for the following 48 hours.

Anaphylaxis may occur as a result of exposure to specific agents (e.g. food, medication, or insect bites/stings).[5] Patients should be educated about specific exposures that may place them at risk for future reactions. They should also be provided counseling on avoidance measures to reduce risk for such exposures. Patients who have had anaphylaxis should carry self-injectable epinephrine for emergency use. These patients should also carry identification indicating they are prone to anaphylaxis and indicate the responsible agent.

Pharmacology

Epinephrine acts on both alpha and beta adrenergic receptors. By acting on the alpha adrenergic receptors, epinephrine reduces vasodilation and increases vascular permeability that occurs during anaphylaxis which alleviates loss of intravascular fluid volume and hypotension. Through its action on beta adrenergic receptors, epinephrine causes bronchial smooth muscle relaxation which alleviates bronchospasm, wheezing, and dyspnea that may occur during

anaphylaxis. Epinephrine may also be useful in reducing urticaria, pruritis, angioedema, and gastrointestinal/genitourinary symptoms associated with anaphylaxis as a result of its relaxing effects on the smooth muscle of the stomach, intestines, uterus, and urinary bladder.

Pharmacokinetics[6]

Drug	Route of Administration	Onset of Action	Duration of Action
epinephrine (Adrenaclick 0.3mg, Adrenaclick 0.15 mg, Epi Pen, Epi Pen Jr., Twinject, Twinject Jr.)	SC	Five to 15 minutes	One to four hours
	IM	Variable	One to four hours

Contraindications/Warnings[7,8,9]

There are no absolute contraindications for use of epinephrine in life-threatening situation. Epi Pen contains sodium metabisulfite. Twinject and Adrenaclick contain sodium bisulfite. The presence of a sulfite in the products should not deter administration of the drug for treatment of serious allergic or other emergency situations even if the patient is sulfite-sensitive.

Drug Interactions[10]

Epinephrine should be used cautiously in patients receiving any of the following drugs: albuterol, dobutamine, dopamine, isoproterenol, metaproterenol, norepinephrine, phenylephrine, phenylpropanolamine, pseudoephedrine, ritodrine, salmeterol, and terbutaline.

Adverse Effects[11]

Adverse reactions to epinephrine include transient, moderate anxiety; apprehensiveness; restlessness; tremor; weakness; dizziness; sweating; palpitations; pallor; nausea/vomiting; headache; and/or respiratory difficulties. Although these reactions may occur in patients receiving therapeutic doses, they are more likely to occur in patients with hypertension or hyperthyroidism. Arrhythmias, including fatal ventricular fibrillation, have been reported in patients with underlying cardiac disease or certain drugs. Rapid rises in blood pressure have produced cerebral hemorrhage, particularly in elderly patients with cardiovascular disease. Angina may occur in patients with coronary artery disease. The potential for epinephrine to produce these types of adverse reactions does not contraindicate its use in an acute life-threatening allergic reaction[12].

Special Populations[13,14,15]

Pediatrics

The self-injectable epinephrine products in this category are approved for use in children based on their weight. Please consult the individual package inserts for specific product information.

Pregnancy

Epinephrine is Pregnancy Category C.

Renal Impairment

There are no specific recommendations for adjustments necessary for patients with impaired renal function. Please consult the individual package inserts for specific product information.

Hepatic Impairment

There are no specific recommendations for adjustments necessary for patients with impaired hepatic function. Please consult the individual package inserts for specific product information.

Dosages[16,17,18]

Drug	**Patient Weight of 30 kg or more (66 pounds or more)**	**Patient Weight of 15 to 30 kg (33 to 66 pounds)**	**Availability** *Special Note: Inject IM or SC in the anterolateral aspect of the thigh, through clothing if necessary.*
epinephrine (Adrenaclick 0.3 mg, Adrenaclick 0.15 mg)	0.3 mg injection	0.15 mg injection	Adrenaclick 0.3 mg (0.3 mL; 1:1000) Adrenaclick 0.15 mg (0.15 mL; 1:1000) Dual packs of both Adrenaclick 0.3 mg and Adrenaclick 0.15 mg are available with two auto-injectors *may be repeated if necessary every 10 to 15 minutes of anaphylaxis* *individual Adrenaclick devices are intended for a single administration*
epinephrine (Epi Pen, Epi Pen Jr.)			Epi Pen 0.3 mg (0.3 mL; 1:1000) Epi Pen Jr. 0.15 mg (0.3 mL; 1:2000) Dual packs of both Epi Pen and Epi Pen Jr. are available with two Auto injectors and one Auto injector trainer device *may be repeated if necessary every 10 to 15 minutes for anaphylaxis* *Individual Epi-Pen devices are intended for a single administration*
epinephrine (Twinject, Twinject Jr.)			Twinject 0.3 mg (0.3 mL; 1:1000) Twinject Jr. 0.15 mg (0.15 mL; 1:1000) Dual packs of both Twinject and Twinject Jr. are available with two Auto injectors and one Demonstrator device *may be repeated if necessary every 10 to 15 minutes for anaphylaxis* *Initial dose is auto-injected and second dose can be manually administered following a partial disassembly of a single Twinject device*

Devices[19,20,21]

These products are intended for immediate self-administration as emergency supportive therapy only and are not a substitute for immediate medical care.

Adrenaclick 0.3 mg and Adrenaclick auto-injectors each contain 1.1 mL of epinephrine solution, of which, one dose can be delivered by auto-injection. Adrenaclick 0.3 mg delivers 0.3 mL of solution in a single dose and Adrenaclick 0.15 mg delivers 0.15 mL of solution in a single dose. The remaining volume after delivery of the fixed dose cannot be administered and should be discarded.

Epi-Pen and Epi-Pen Jr. Auto Injectors each contain two mL of epinephrine solution. Approximately 1.7 mL remains unusable after activation. Each Epi-Pen delivers 0.3 mg epinephrine in a single dose. Each Epi-Pen Jr. delivers 0.15 mg epinephrine in a single dose.

Twinject auto-injector contains 1.1 mL of epinephrine solution from which two doses of either 0.15 mg (0.15 mL) or 0.3 mg (0.3 mL) each is available for use by injection. The first dose is administered via auto-injection by the patient. A second dose can be manually administered following a partial disassembly of Twinject. The remaining volume is not available for use and should be discarded.

Clinical Trials

Studies were identified through searches performed on PubMed and review of information sent by manufacturers. Search strategy included the FDA-approved use of all drugs in this class. Randomized, comparative, controlled trials comparing agents within this class for the approved indications are considered the most relevant in this category. Studies included for analysis in the review were published in English, performed with human participants and randomly allocated participants to comparison groups. In addition, studies must contain clearly stated, predetermined outcome measure(s) of known or probable clinical importance, use data analysis techniques consistent with the study question and include follow-up (endpoint assessment) of at least 80 percent of participants entering the investigation. Despite some inherent bias found in all studies including those sponsored and/or funded by pharmaceutical manufacturers, the studies in this therapeutic class review were determined to have results or conclusions that do not suggest systematic error in their experimental study design. While the potential influence of manufacturer sponsorship/funding must be considered, the studies in this review have also been evaluated for validity and importance.

There are no comparative trials currently available for the self-injectable epinephrine products.

Summary

Anaphylaxis is a life-threatening allergic reaction that can be caused by a variety of allergens including food, medications, insect stings and bites, and latex. All patients at risk of anaphylaxis are urged to carry self-injectable epinephrine (Adrenaclick 0.3mg, Adrenaclick 0.15 mg, Epi-Pen, Epi-Pen Jr., Twinject, or Twinject Jr.). Patients should be well informed by their physician and/or pharmacist of when to use this life saving medication.

The Twinject device differs from the Epi-Pen device by allowing the patient to deliver two doses instead of a single dose from one unit. Initial doses from either of the devices are delivered via auto-injection. However, Twinject devices allow for manual injection of a second dose upon partial disassembly of the device.

References

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