

Emergency Epinephrine Devices

modified September 2024

In addition to the well-known *EpiPen*, there are several other emergency epinephrine devices to treat anaphylaxis.^{1,2,7} *Auvi-Q*'s (US) 0.1 mg auto-injector is marketed to have a lower risk of adverse effects (e.g., tremor, heart palpitations) in younger patients. It also has a smaller needle, designed to penetrate more often into muscle rather than bone in younger patients. *Emerade* (Canada) offers a 0.5 mg strength which is marketed as an option for heavier patients.⁸ However, data are lacking to support the benefits of these newer strengths over the well-used 0.15 mg and 0.3 mg strengths. *Symjepi* (US) is a prefilled syringe that is proposed to be more intuitive than an autoinjector since patients see the needle and depress the plunger themselves.³⁷ *Neffy* (US) is a nasal spray which may be an option for some patients with a fear of needles. With high costs, shortages and recalls, generics, new strengths, a prefilled syringe, and a nasal spray; there are lots of questions about the different formulations and which one a patient should use. The choice between devices is determined by insurance coverage, availability, and ease of use. This document answers frequently asked questions about emergency epinephrine devices.

Note: Anaphylaxis is a potentially life-threatening condition. No matter which device is prescribed, all patients should be instructed on the appropriate, immediate use of their product. They should also be instructed to seek immediate medical attention (i.e., call 911) after epinephrine administration. Patients should always have two emergency epinephrine devices available in case a second dose is required during an anaphylactic reaction.

Question	Answer/Pertinent Information
Which emergency epinephrine devices are available?	Emergency epinephrine injection devices come in several strengths and are dispensed based on the patient's weight: <ul style="list-style-type: none"> • Most injection devices: 0.3 mg (30 kg and greater) and 0.15 mg (<30 kg). • <i>Auvi-Q</i> (US): also has 0.1 mg (7.5 kg to 15 kg). • <i>Emerade</i> (Canada): also has 0.5 mg (an option for adults >60 kg, based on clinical judgment).⁴¹ Note that <i>Emerade</i> 0.15 mg strength has been approved but is not marketed at the time of publication. <p><i>EpiPen, EpiPen Jr:</i> The auto-injector is packaged in a tube-like carrier about five and a half inches long.⁷</p> <ul style="list-style-type: none"> • Epinephrine injection, USP auto-injector (US; Mylan Specialty) is the authorized generic for <i>EpiPen, EpiPen Jr</i>.^{19,32} • Epinephrine auto-injector (US; Teva Pharmaceuticals USA) is an AB-rated generic for <i>EpiPen</i> and <i>EpiPen Jr</i>.⁹ <p><i>Adrenaclick</i> (US) is a cylindrical device, similar in length and size to the <i>EpiPen</i>.⁷</p> <ul style="list-style-type: none"> • Epinephrine injection, USP auto-injector (US; Impax Generics) is the authorized generic for <i>Adrenaclick</i>.²⁷ <p><i>Auvi-Q</i> (US), <i>Allerject</i> (Canada): Credit card-sized (~3.5 x 2 inches) device with audio cues during administration.^{5,7}</p> <p><i>Symjepi</i> (US) is a prefilled syringe, about four inches in length.^{29,37}</p>

Question	Answer/Pertinent Information
<p><i>Continued...</i> Epinephrine devices, continued</p>	<p>Emerade (Canada) is an auto-injector, packaged in a tubular protective case, similar in size to the <i>EpiPen</i>.⁴¹</p> <ul style="list-style-type: none"> • Has a longer needle compared to other epinephrine injection devices. Promoted to more consistently deliver epinephrine intramuscularly rather than subcutaneously (i.e., through clothing and excess subcutaneous tissues).⁴² • In May 2023, all <i>Emerade</i> auto-injectors were recalled due to risk of premature activation or of failure to activate. Date for return to market is unknown.⁴⁴ <p>Neffy (US) is a 2 mg, one-dose nasal spray indicated for patients 30 kg and more.</p>
<p>Are there any alternatives to epinephrine injection devices?</p>	<p>Epinephrine kits: Vials or ampules of epinephrine in a kit with two doses, needles, and syringes.</p> <ul style="list-style-type: none"> • May be considered as a last resort for someone in the community who is unable to afford injection devices.¹⁸ • Cost for an assembled kit is estimated at ~\$20. • May be a better option for institutions, clinics, etc (rather than patients) where clinicians are familiar with using syringes and needles. • May increase the risk for dosing errors and delay in treatment. Directions should be included in the kit with the dose and route of administration in bold print. • Filter needles may be needed if epinephrine ampules are used in the kit. Ensure you are providing the correct size needle for your patient with our chart, <i>Choosing the Correct Needle Size</i>. • For settings using epinephrine frequently, preparing syringes ahead of time may be helpful. <ul style="list-style-type: none"> • Pre-made syringes may be stable two to three months if protected from heat and light.^{22,23} • Epinephrine should be given intramuscularly (rather than subcutaneously) for treatment of anaphylaxis for the fastest absorption.²⁸ • If dispensed to a patient in the community, patients must be: <ul style="list-style-type: none"> • reliable, trained, highly-motivated, and comfortable with the process. • able to accurately measure the dose and be trained to not use the entire vial. • Some emergency medical services (EMSs) are now stocking kits rather than <i>EpiPens</i>.²⁴ <ul style="list-style-type: none"> • reduces costs. • appears to increase appropriate use of epinephrine due to less hesitation about whether or not a reaction is serious enough to use a more costly epinephrine injection device. • <i>epinephrinesnap</i>, <i>epinephrinesnap-EMS</i>, and <i>epinephrinesnap-v</i> (US only).²⁵ <ul style="list-style-type: none"> • commercial kits available for healthcare professionals. • contains a vial of epinephrine 1 mg/mL, needles, syringes, alcohol pads, labels, and instructions. • training kits are also available. • cost is ~\$90.

Question	Answer/Pertinent Information
What are some of the new products on the horizon?	<p>Alternate modes of epinephrine administration (i.e., sublingual) are being studied.⁴³</p> <ul style="list-style-type: none"> • Clinical data is still lacking for most formulations, especially in pediatric patients and comparison studies.
Are epinephrine injection devices interchangeable?	<p>US:</p> <ul style="list-style-type: none"> • Teva’s epinephrine auto-injector is AB-rated to <i>EpiPen</i> and <i>EpiPen Jr.</i>, and is interchangeable.²⁶ • <i>Adrenaclick</i> and <i>Auvi-Q</i> epinephrine injection devices have a therapeutic equivalence rating of BX (i.e., data are insufficient to determine therapeutic equivalence).⁹ • Some states may allow interchanges of these products as governed by their state law.¹⁰ • Two of the generic formulations, “epinephrine injection, USP auto-injector,” (Mylan and Impax Generics) are authorized generics of <i>EpiPen</i> and <i>Adrenaclick</i>, respectively. This means that <i>EpiPen</i> and <i>Adrenaclick</i> have been relabeled and marketed under the generic product name. These generic products are identical to their respective brand name products. However, their automatic substitution is determined by individual state law.¹¹ • <i>Symjepi</i> is not interchangeable with the other epinephrine injection devices. <p>Canada:</p> <ul style="list-style-type: none"> • Follow provincial and territorial laws; <i>EpiPen</i>, <i>Allerject</i>, and <i>Emerade</i> are not usually interchangeable. <p>One small pharmacokinetic study compared <i>EpiPen</i> to <i>Auvi-Q</i> in 69 healthy people. They demonstrated bioequivalence between these two products.¹²</p>
What is the cost of each epinephrine device?	<p>Cost for packages of two devices:^a</p> <ul style="list-style-type: none"> • <i>EpiPen</i> or <i>EpiPen Jr.</i>: \$610 (\$190 in Canada) • <i>Auvi-Q</i> (US): \$620 • <i>Allerject</i> or <i>Allerject Jr.</i> (Canada): \$205 • <i>Adrenaclick</i> (US): \$460 • <i>Adrenaclick</i> authorized generic epinephrine auto-injector, USP (US): \$300 • <i>EpiPen</i> authorized generic epinephrine auto-injector, USP (US): \$300 • Epinephrine auto-injector (US; Teva): \$300 • <i>Symjepi</i> (US): \$250 • <i>Emerade</i> (Canada): \$175 • <i>Neffy</i> (US): \$710 <p>NOTE: Pricing between products varies based on discounts from individual pharmacies, insurance plans, and manufacturers.</p> <p>Reduced and \$0 co-pay cards are available from most US manufacturers, for example (all information below is subject to change):</p> <p><i>Continued...</i></p>

Question	Answer/Pertinent Information
Cost of epinephrine devices, continued	<ul style="list-style-type: none">• An <i>EpiPen</i> \$300 savings card (US only) for out-of-pocket costs is available for eligible patients. This online card (https://www.activatethecard.com/viatrisadvocate/epipen/welcome.html) can be printed or stored on a smartphone for presentation at a pharmacy. They also offer a Patient Assistance Program (for low income families) and an <i>EpiPen4Schools</i> program (for eligible schools) for <i>EpiPen</i> and its authorized generic (https://www.epipen.com/paying-for-epipen-and-generic).• <i>EpiPen</i>'s authorized generic epinephrine auto-injector (US only) offers a \$25 off savings card to eligible patients, available online (https://www.activatethecard.com/mylanadvocate/mygenericeai/welcome.html).• <i>Adrenaclick</i>'s authorized generic epinephrine auto-injector (US only) offers a \$0 co-pay coupon for patients with insurance and a \$10 off savings coupon for cash paying customers. Their online card can be printed, then taken to the pharmacy or mailed for the rebate (https://sservices.trialcard.com/Coupon/Epinephrine).• <i>Auvi-Q</i> (US only) offers \$35 co-pay for commercially insured patients. They also offer a Patient Assistance Program which offers <i>Auvi-Q</i> free of charge for eligible patients (https://www.auvi-q.com/get-auvi-q).• Generic epinephrine (Teva, US only) offers a \$30 savings card to eligible patients (https://www.tevaepinephrine.com/globalassets/epipen/pdfs/tg-43298_epinephrine-injection-usp-auto-injectors-digital-copay-card---2023-update_final.pdf).• <i>Symjepi</i> (US only) offers copay support (\$0 for eligible patients) and up to \$100 off for cash paying customers (https://portal.trialcard.com/usworldmeds/symjepi/).• <i>Neffy</i> (US only) offers a co-pay savings program (as low as \$25 if eligible) and a patient assistance program (\$0 for eligible patients) (https://www.neffy.com/savings-and-support/)
What is the role for training devices?	<p>Epinephrine devices are often used incorrectly, even by healthcare professionals.^{5,14,15}</p> <ul style="list-style-type: none">• Each epinephrine device has a different administration technique so the instructions for proper use vary.¹⁰• Patients must be trained and educated on the use of their device. Repeat with every prescription filled/refilled.^{10,14}• Ask your patients if they have had training on a device and try to dispense the same device if possible.¹⁰• Be sure that the patient understands if their device has changed and has new administration instructions.• For interchanged or new devices, patients must be retrained. <p>Patients must be trained on correct administration technique.⁵</p> <ul style="list-style-type: none">• Demonstrate with a training device when available and then have the patient practice.• Training devices resemble the actual device but do not contain medication or a needle (for injectables).• Training devices can be used more than once so that patients, parents, and caregivers can all repeatedly practice proper administration.• Consider ordering training devices to have on hand in your pharmacy or office for teaching purposes.

Continued...

Question	Answer/Pertinent Information
<p>Training devices, continued</p>	<p>A training device is included with each <i>EpiPen</i> and its generic product two pack.^{3,19} Additional trainers can be obtained by calling 800-395-3376.</p> <p><i>Adrenaclick</i> and its generic product don't come with a training device, but training devices are available. They can be ordered online at http://epinephrineautoinject.com/order-product-trainers/, by calling 855-EPINEPH, or by mailing the form found inside the device package.⁶</p> <p>A training device is included with each <i>Auvi-Q</i> two pack. Additional trainers are available at www.auvi-q.com.¹⁶ Free training devices are available for <i>Allerject</i> (www.allerject.ca) and <i>Emerade</i> (www.emerade.ca).</p> <p>NOTE: Training devices are only available for epinephrine auto-injectors, not for the <i>Symjepi</i> prefilled syringe.</p> <p><i>Neffy</i> (US) does not come with a training device, but training devices are available. They can be ordered online at https://www.neffypro.com/#sign-up.</p>
<p>How do epinephrine injection devices differ?</p>	<p>Safety caps:</p> <ul style="list-style-type: none"> • The <i>EpiPen</i>, its authorized generic, and the Teva generic auto-injectors all have one blue safety cap to remove at the non-needle end of the device.^{3,19,38} • <i>Auvi-Q</i> and <i>Allerject</i> have a red safety guard to remove prior to use.^{16,36} • The <i>Adrenaclick</i> and its generic have one blue cap at each end to remove prior to use.^{6,31} • <i>Symjepi</i> has a blue cap that must be pulled off to expose the needle prior to use.²⁹ • <i>Emerade</i> has a needle cap/shield that must be removed prior to use.⁴¹ <p>Epinephrine injection devices are recommended to be given into the outer thigh for fastest absorption.</p> <ul style="list-style-type: none"> • Consider the length of time the device must be held in place on the thigh when choosing, particularly for children: <ul style="list-style-type: none"> • <i>EpiPen</i>, its authorized generic, and the Teva generic's recommended motion is to "swing and push," then hold in place for three seconds.^{3,17,19,30,38} • <i>Auvi-Q</i> is recommended to be pressed firmly and held in place for two seconds.¹⁶ • <i>Allerject</i> is recommended to be pressed firmly and held in place for five seconds.³⁶ • <i>Adrenaclick</i> and its generic are recommended to be pressed and held firmly in place for ten seconds.^{6,31} • <i>Symjepi</i> should be injected downwards into the thigh while the patient is sitting. Once the needle is inserted, the plunger should be pushed down until it clicks and then held in place for two seconds.²⁹ • <i>Emerade</i> should be pressed firmly, then held in place for five seconds.⁴¹

Question	Answer/Pertinent Information
How is emergency epinephrine nasal spray (<i>Neffy</i>) used?	Epinephrine nasal spray (<i>Neffy</i>) is for single use, with the entire dose administered upon activation. ⁴⁶ <ul style="list-style-type: none">• Device is ready to use once removed from packaging.• Either nostril can be used for administration. If a second dose is necessary, after five minutes, a new spray should be administered into the same nostril as the initial dose.⁴⁶• Nasal device should not be primed or tested as this will discharge the dose.• Can be administered to a patient in any position (sitting, standing, lying down).
What is the shelf life of epinephrine devices?	The usual expiration date for epinephrine injection devices is 15 to 20 months from date of manufacture. <i>Neffy</i> nasal spray has a usual expiration of 30 months from date of manufacture and appears to be more stable to extreme heat exposure compared to <i>EpiPen</i> and <i>Symjepi</i> . ^{45,47} <ul style="list-style-type: none">• Good inventory control can help ensure most patients have about a year (or more) before their next refill.• Patients should check the expiration date of their device to know when they'll need a refill. Some devices have a window to see the solution. If the solution is discolored or contains particles, the device should be replaced (regardless of the expiration date).• Many pharmacies, as well as the <i>EpiPen</i> website, offer refill reminders. Many of these devices expire before a patient needs to use them. <ul style="list-style-type: none">• In response to previous decreased supplies of epinephrine auto-injectors and based on new stability data, the FDA authorized an extension of the expiration date of some specific lots of the 0.3 mg <i>EpiPen</i> and its authorized generic by four months.³⁴• For all other epinephrine injection devices not included in the FDA's expiration date extension, recently expired devices may lose some of their potency and shouldn't be relied on to treat a reaction.• If a patient is having an anaphylactic reaction, it may be preferable to use a recently expired device rather than not give any epinephrine at all.^{13,21} Encourage patients to store their epinephrine devices properly. One small pilot study of the injections suggests that epinephrine concentrations may be reduced by up to 14% when the devices are left in a car's glovebox for 12 hours on a hot day. ³⁹

Question	Answer/Pertinent Information
Are there risks associated with use of emergency epinephrine devices?	<p>There are no contraindications to the use of emergency epinephrine devices.^{20,29}</p> <p>Accidental self-injection with these devices is not uncommon.</p> <ul style="list-style-type: none">• The device is sometimes held the wrong way, causing the thumb to be punctured rather than the thigh.¹⁵• <i>Auvi-Q</i> and <i>Allerject</i> are designed so the needle end is more easily identified, making them less likely to be held incorrectly.¹⁷• Patients can see the needle with <i>Symjepi</i>, which may make it less likely to be held incorrectly.• <i>Emerade</i> has an obvious opening at the needle end where the sheath is removed, and none on the opposite end.⁴¹ <p>There are reports of lacerations and embedded needles caused by epinephrine auto-injector use and misuse, mainly in children.¹ Needle exposure once administration is complete:</p> <ul style="list-style-type: none">• After use, the <i>EpiPen</i>, its authorized generic, and the Teva generic’s orange tip extends to cover the needle.^{3,19,38}• <i>Auvi-Q</i> and <i>Allerject</i> have a retractable needle system and safety tab mechanism located on the same end as the needle.⁵• The needle remains exposed on the <i>AdrenaClick</i> and its generic.^{6,31} The device should be put back into the carrying case, needle first.^{6,31}• After use, the needle of the <i>Symjepi</i> prefilled syringe should be covered by sliding the safety guard over the needle until it clicks.²⁹• After use, a protective sheath covers the needle of the <i>Emerade</i> auto-injector.⁴¹ <p>There have been reports of the auto-injector labels sticking to the carrier tubes of the <i>EpiPen</i>, <i>EpiPen Jr</i>, and their authorized generics. This could cause a delay in the administration of the auto-injector. Pharmacists and patients should make sure auto-injectors can be easily removed from their outer tubes prior to dispensing and prior to when they need to use them, respectively.⁴⁰</p>

a. Pricing is wholesale acquisition cost (WAC). US medication pricing by Elsevier, accessed January 2024 (September 2024 for *Neffy*).

Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

Levels of Evidence

In accordance with our goal of providing Evidence-Based information, we are citing the **LEVEL OF EVIDENCE** for the clinical recommendations we publish.

Level	Definition	Study Quality
A	Good-quality patient-oriented evidence.*	<ol style="list-style-type: none"> 1. High-quality randomized controlled trial (RCT) 2. Systematic review (SR)/Meta-analysis of RCTs with consistent findings 3. All-or-none study
B	Inconsistent or limited-quality patient-oriented evidence.*	<ol style="list-style-type: none"> 1. Lower-quality RCT 2. SR/Meta-analysis with low-quality clinical trials or of studies with inconsistent findings 3. Cohort study 4. Case control study
C	Consensus; usual practice; expert opinion; disease-oriented evidence (e.g., physiologic or surrogate endpoints); case series for studies of diagnosis, treatment, prevention, or screening.	

***Outcomes that matter to patients** (e.g., morbidity, mortality, symptom improvement, quality of life).

[Adapted from Ebell MH, Siwek J, Weiss BD, et al. Strength of Recommendation Taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. *Am Fam Physician* 2004;69:548-56. <https://www.aafp.org/pubs/afp/issues/2004/0201/p548.html>.]

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Cite this document as follows: Clinical Resource, Emergency Epinephrine Injection Devices. Pharmacist's Letter/Pharmacy Technician's Letter/Prescriber Insights. January 2024. [400164]

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