

Emergency Epinephrine Injection Devices

The *EpiPen* is the most well-known epinephrine injection device. However, there are several other epinephrine injection devices available in the U.S. The *EpiPen* was the first one available and maintains over 90% of the market.¹ A generic *EpiPen* is available in the U.S., joining authorized generics for *EpiPen* and *Adrenacllick*.² *Auvi-Q*'s newest strength (0.1 mg) is marketed to have a lower risk of adverse effects in younger patients (e.g., tremor, heart palpitations, etc). It also has a smaller needle designed to penetrate more often into muscle rather than bone in these younger patients. Data is lacking to support these benefits over the well-used 0.15 mg strength. The newest product, *Symjepi*, is prefilled syringe that is proposed to be more intuitive than an autoinjector since patients see the needle and depress the plunger themselves.³⁷ There are also numerous spot shortages of various epinephrine injection devices. With the high costs of epinephrine injection devices, shortages, various generics, new strength, and new prefilled syringe; there are lots of questions about the differences between the epinephrine injection devices, which device patients should use, and if there are any alternatives. The choice between devices will be determined by insurance coverage, availability, and ease of use. This document will address frequently asked questions about epinephrine injection devices.

Note: Anaphylaxis is a potentially life-threatening condition. No matter which injection 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 injection devices available in case a second dose is required during an anaphylactic reaction.

Clinical question	Pertinent information
<p>Which epinephrine injection devices are available?</p> <p><i>Continued...</i></p>	<p>Epinephrine injection devices come in three strengths (two in Canada) and are dispensed based on the patient's weight: Most injection devices: 0.3 mg (30 kg and greater) and 0.15 mg (<30 kg) <i>Auvi-Q</i>, only (U.S.): 0.3 mg (30 kg and greater), 0.15 mg (15 kg to 30 kg), and 0.1 mg (7.5 kg to 15 kg)</p> <p><i>EpiPen</i>: The auto-injector is packaged in a tube-like carrier about five inches long.³</p> <ul style="list-style-type: none"> • “Epinephrine injection, USP auto-injector” (U.S.; Mylan Specialty L.P.) is the authorized generic for <i>EpiPen</i> and <i>EpiPen Jr</i>.³² • Epinephrine auto-injector (U.S.; Teva Pharmaceuticals USA) is an AB-rated generic for <i>EpiPen</i> and <i>EpiPen Jr</i>.³⁸ <p><i>Adrenacllick</i> (U.S.; brand no longer manufactured) is a cylindrical device, similar in length and size to the <i>EpiPen</i>.³¹</p> <ul style="list-style-type: none"> • “Epinephrine injection, USP auto-injector” (U.S.; Impax Generics/Lineage Therapeutics) is the authorized generic for <i>Adrenacllick</i>.⁶

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Clinical question	Pertinent information
<p>Availability of epinephrine injection devices, continued</p>	<p>Auvi-Q (U.S.), Allerject (Canada, not currently available): Credit card-sized device with audio cues during administration.⁵</p> <ul style="list-style-type: none"> • Recalled in both Canada and the U.S. in 2015 due to a risk for inaccurate dose delivery. In 2017, <i>Auvi-Q</i> returned to the U.S. market while <i>Allerject</i> continues to be unavailable in Canada. • In August 2018, Health Canada authorized the temporary importation of <i>Auvi-Q</i> auto-injectors to Canadian pharmacies in response to shortages of <i>EpiPen</i> and <i>EpiPen Jr.</i> Note that <i>Auvi-Q</i> does not have French labelling or instructions.³⁶ Patient information for <i>Auvi-Q</i> is available via Health Canada in both English and French (https://www.canada.ca/fr/sante-canada/services/medicaments-produits-sante/medicaments/annonces/auvi-q-renseignements-patient.html). <p>Symjepi (U.S.) is a prefilled syringe, about four inches in length.^{29,37}</p> <ul style="list-style-type: none"> • Available initially as the 0.3 mg strength, with the 0.15 mg strength expected to follow soon after.
<p>Are there any alternatives to epinephrine injection devices?</p> <p><i>Continued...</i></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 <ul style="list-style-type: none"> • If dispensed to a patient in the community: • Patients must be reliable, trained, highly-motivated, and comfortable with the process. • Patients must be 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.

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<p>Alternatives to epinephrine injection devices, continued</p>	<ul style="list-style-type: none"> • <i>epinephrinesnap-EMS</i> and <i>epinephrinesnap-v</i> (U.S. only).²⁵ <ul style="list-style-type: none"> • Commercial kit available for healthcare professionals. • Contains vial of epinephrine 1 mg/mL, needles, syringes, alcohol pads, labels, and instructions. • Training kits are also available. • Cost is \$130 to \$150.
<p>What is the <i>Veta Smart Case</i>?</p>	<ul style="list-style-type: none"> • <i>Veta Smart Case</i>⁷ <ul style="list-style-type: none"> • Reusable, transparent case for the <i>EpiPen</i>, <i>EpiPen Jr</i>, or Mylan’s authorized generics for <i>EpiPen</i> and <i>EpiPen Jr</i>. • Monitors and sends alerts for out-of-range temperature, location, separation of case from the smart device, the removal of the <i>EpiPen</i> from the case, expiration date of the <i>EpiPen</i>, etc. • Alerts can be customized to go to the user and people in their support circle (e.g., parents, caregivers, etc). • Uses Bluetooth technology to connect to an app on smart devices (Apple or Android). • Cases cost \$129 USD (\$149 CAD) each or \$169 USD (\$199 CAD) for two. • A one-year subscription to the app is included with each case. The annual subscription cost is \$24 USD per case, to a maximum of \$48 USD annually for four or more cases. A subscription is not required; however, without a subscription, only the person carrying the case receives notifications and alerts.
<p>What are some of the new products on the horizon?</p>	<p>Several new devices currently in development:</p> <ul style="list-style-type: none"> • INSYS Therapeutics is developing an epinephrine nasal spray which has been granted an FDA Fast Track designation. They project filing a New Drug Application (NDA) to FDA by the fourth quarter of 2019.³⁵ • Windgap Medical’s auto-injector, <i>Abiliject</i>, is expected to be submitted to the FDA soon.²⁷ <ul style="list-style-type: none"> • Small (about the size of a lipstick tube). Fits easily into a pocket.²⁷ • Formulated with a dry powder. Reconstitutes when the twist-off end is removed just prior to administration. <ul style="list-style-type: none"> • Longer shelf-life (up to double that of existing products).²⁷ • Less susceptible to temperature changes than the currently available solution-containing devices.²⁷ • Designed so that the end with the needle is very easily recognized. This may decrease the inadvertent injection into the thumb seen with current devices.^{8,27} • <i>AdrenaCard</i> is an auto-injector the size of a credit card and can fit into some wallets. It had been projected to be on the market by 2018.⁴ • Imprimis Pharmaceuticals is working on a customizable epinephrine auto-injector compounding kit for less than \$100.^{32,33}

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<p>Are epinephrine injection devices interchangeable?</p>	<p>U.S.</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/Lineage Therapeutics) 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"> • <i>EpiPen</i> and <i>Allerject</i> (prior to recall) are not 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>
<p>What is the cost of each epinephrine injection device?</p>	<p>Cost for packages of two injection 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> (U.S.): \$4,900. • <i>Adrenaclick</i> authorized generic epinephrine auto-injector, USP (U.S.): \$395. • <i>EpiPen</i> authorized generic epinephrine auto-injector, USP (U.S.): \$300. • Epinephrine auto-injector (U.S.; Teva): \$300. • <i>Symjepi</i> (U.S.): \$250. <p>NOTE: Pricing between products may vary based on discounts from individual pharmacies, insurance plans, and manufacturers.</p> <p>Reduced and \$0 co-pay cards are available from some manufacturers (note that discounts and prices are subject to change).</p> <ul style="list-style-type: none"> • <i>EpiPen</i> (U.S. only) offers a \$300 savings card for out-of-pocket costs for eligible patients. This online card can be printed or stored on a smartphone for presentation at a pharmacy (https://www.activatethecard.com/epipen/). Mylan also offers 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 (U.S. only) offers a \$25 off savings card to eligible patients, available online (https://www.activatethecard.com/mygenericeai/?_ga=1.156437051.1627760818.1483644964).

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Clinical question	Pertinent information
<p>Cost of epinephrine injection devices, continued</p>	<ul style="list-style-type: none"> • <i>Adrenaclick</i>'s authorized generic epinephrine auto-injector (U.S. only) offers a \$0 co-pay coupon for patients with insurance and a \$25 off savings coupon for cash paying customers. Their online card can be printed, then taken to the pharmacy or mailed for the rebate (https://services.trialcard.com/Coupon/Epinephrine). • <i>Auvi-Q</i> (U.S. only) offers \$0 out-of-pocket cost for all commercially insured patients. They also offer a Patient Assistance Program which offers <i>Auvi-Q</i> free of charge for patients with a household income of less than \$100,000 who do not have insurance (https://www.auvi-q.com/getting-auvi-q/).
<p>What is the role for auto-injector training devices?</p>	<p>Epinephrine devices are often used incorrectly, even by healthcare professionals.^{5,14,15}</p> <ul style="list-style-type: none"> • Each epinephrine injection 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 a needle. • Training devices can be used more than once so that patients, parents, caregivers, etc can all repeatedly practice proper administration. <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. <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 Consider ordering some to have on hand in your pharmacy or office for teaching purposes.</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</p> <p>NOTE: Training devices are only available for epinephrine auto-injectors, not for the <i>Symjepi</i> prefilled syringe.</p>

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<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> has a red safety guard to remove prior to use.¹⁶ • The <i>AdrenaClick</i> auto-injector has one grey cap at each end to remove prior to use.³¹ Its generic has one blue cap at each end to remove prior to use.⁶ • <i>Symjepi</i> has a blue cap that must be pulled off to expose the needle prior to use.²⁹ <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 and held in place for two seconds.¹⁶ • <i>AdrenaClick</i> and its generic auto-injector are recommended to be held 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
<p>What is the shelf life of epinephrine injection devices?</p>	<p>The usual expiration date for epinephrine injection devices is 15 to 20 months from date of manufacture.</p> <ul style="list-style-type: none"> • Good inventory control can help ensure most patients have about a year before their next refill. • Patients should check the expiration date of their device to know when they’ll need a refill. 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. <p>Many of these devices expire before a patient needs to use them.</p> <ul style="list-style-type: none"> • In response to decreased supply of epinephrine auto-injectors and based on new stability data, the FDA has authorized an extension of the expiration date of some lots of the 0.3 mg <i>EpiPen</i> and its authorized generic by four months. Specific lot information can be found on the FDA’s website (https://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm563360.htm).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} <p>Encourage patients to store their epinephrine injection devices properly. One small pilot study 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</p>

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<p>Are there risks associated with use of epinephrine devices?</p>	<p>There are no contraindications to the use of epinephrine injection 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> is designed so the needle end is more easily identified, making it 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. <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> has 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> device and its generic auto-injector.^{6,31} The device should be put back into the carrying case, needle first.⁶ • 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 <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). Medication pricing by Elsevier, accessed January 2019 (for U.S. pricing)

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.

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