



March 23, 2020

Important Prescribing Information

Subject: Important Safety Information on the EpiPen® and EpiPen Jr® Auto-Injectors and their authorized generic versions:

- **Risk of device failure due to spontaneous activation.**
- **Difficulty removing the device from the carrier tube may also occur.**
- **Use errors.**

These issues could delay or prevent emergency treatment when needed.

Dear Healthcare Provider,

The purpose of this letter is to inform you that the administration of EpiPen® 0.3 mg and EpiPen Jr® 0.15 mg Auto-Injectors and the authorized generic versions (referenced collectively as EpiPen in the remainder of this letter) may be delayed or prevented during an emergency due to:

1. Device failure from spontaneous activation caused by using a sideways force to remove the blue safety release.
2. Device failure from inadvertent or spontaneous activation due to a raised blue safety release
3. Difficulty removing the device from the carrier tube.
4. Certain identified use errors.

Additional detail around the identified issues is provided below.

Since EpiPen is administered for severe and potentially life-threatening allergic reactions, anything that prevents or delays the administration of the intended dose of epinephrine could result in a high risk to the patient, including the risk of death.

Your patients should continue to carry their EpiPen or EpiPen Jr or authorized generic version at all times, and we encourage you to review the information below with your patients and their caregivers to ensure its appropriate use. Per the instructions for use, we recommend that patients always carry two EpiPen or EpiPen Jr auto-injectors or the authorized generic version at all times. Please refer to the important training reminders enclosed in this letter and precautionary handling instructions for healthcare providers and patients/caregivers, including pictures of the auto-injector, included in Appendix 1. This letter is being issued with the knowledge of the FDA.

1. Device Failure from Spontaneous Activation Caused by Using a Sideways Force to Remove the Blue Safety Release

- Removing the blue safety release using sideways forces has been shown to activate the EpiPen prematurely. If spontaneous activation occurs, the device cannot be used to inject epinephrine; a new device must be obtained.
 - This can occur if a user tries to hold the EpiPen with only one hand and tries to remove the blue safety release with their thumb using a lateral force. As an example, **parents who are administering EpiPen to their children should first restrain their child, then use both**

hands to hold the EpiPen and remove the blue safety release with the other hand straight up without bending, twisting or applying horizontal force.

- **To prevent this premature activation, patients and their caregivers should be advised of the following:**
 - Do NOT flip the blue safety release off using a thumb or by pulling it sideways or bending and twisting. This may cause the device to spontaneously activate: a “click” is heard, the orange needle tip is extended, and the window is blocked. An activated device cannot be used for a patient. If this occurs, obtain a new EpiPen.
 - **Use both hands to remove the blue safety release.** Hold the EpiPen auto-injector in one fist with the orange end pointing down, while removing the blue safety release with the other hand straight up without bending, twisting or applying horizontal force.
 - **Healthcare providers should instruct parents who are administering EpiPen to their children to first restrain the child and then use both hands to remove the blue safety release.**

2. Device Failure from Inadvertent or Spontaneous Activation Due to a Raised Blue Safety Release

- In a very limited number of cases, EpiPen devices may have a blue safety release that is slightly raised.
- The function of the blue safety release is to ensure the device does not activate prior to its intended use.
- If the blue safety release is raised (see Appendix 1), the device may activate prematurely, which could potentially delay or prevent emergency treatment when needed.
- **To prevent this spontaneous activation, pharmacists, patients, and their caregivers should be advised of the following:**
 - When dispensing or receiving an EpiPen or EpiPen Jr Auto-Injector or authorized generic, and prior to using the device, visually inspect the auto-injectors to confirm the blue safety release is not raised (see Appendix 1, Steps 1 through 5 for more details including pictures).
 - If the blue safety release is raised, the auto-injector should NOT be dispensed or used since premature activation may occur. Contact Mylan Customer Relations at 1-800-796-9526 to obtain a replacement device(s) at no additional cost.

3. Difficulty Removing the Device from the Carrier Tube

- In some (approximately 0.0002% or 2 parts per million units based on the internal manufacturing process occurrence rate) cases, EpiPen devices may not slide out of their carrier tube easily or potentially at all, which could potentially delay or prevent emergency treatment.
- This issue is related to a slight deformation on the open rim of the plastic carrier tube that may be present but may not be visually obvious to patients/caregivers.
- The probability of an auto-injector that may have a deformity that could cause a delay in release from the carrier tube is very low.
- This issue may affect any EpiPen auto-injector lot currently on the market in the U.S. with the labeled expiry on the device and carton prior to September 2020.

- **To ensure the device can be used when needed, pharmacists, patients, and their caregivers should be advised of the following:**
 - When dispensing or receiving an EpiPen or EpiPen Jr Auto-Injector or authorized generic, and prior to using the device: remove both carrier tubes from the S-clip, flip open the caps of the carrier tubes, and tip each carrier tube to verify that each auto-injector readily slides out of the tube (see Appendix 1, Steps 2, 3 and 4 for more details including pictures).
 - If the auto-injectors do not readily slide from the carrier tubes, they should NOT be dispensed or used. Contact Mylan Customer Relations at 1-800-796-9526 to obtain a replacement device(s) at no additional cost.

4. Certain Identified Use Errors

Through a study examining use by intended users in expected use environments as well as a thorough review of post marketing information, Pfizer, whose subsidiary Meridian Medical Technologies manufactures EpiPen, identified that certain use errors have occurred.

Use Errors	Correct Administration/Important Reminders
✗ Failing to remove the device from the carrier tube prior to use.	✓ EpiPen must be removed from the carrier tube it is provided in prior to use.
✗ Failing to remove the blue safety release prior to use.	✓ EpiPen will not activate with the blue safety release in place.
✗ Activating the auto-injector upside down, resulting in hand injections.	✓ The needle exits from the orange end of the EpiPen which should be in contact with the outer thigh (upper leg) at a right angle (perpendicular) to the thigh prior to, and during activation. The orange needle tip will extend to cover the needle after activation. If the needle is still visible, do not attempt to reuse it.
✗ Failing to apply sufficient force to activate EpiPen.	✓ EpiPen should be administered by swinging and pushing firmly against the outer thigh until it “clicks.” The click signals that injection has started. The correct dose has been administered if the orange needle tip is extended and the window is blocked.
✗ Administering at a site other than the outer thigh.	✓ Administer EpiPen in the outer thigh only.
✗ Failing to hold the auto-injector in place for a full three seconds.	✓ Hold EpiPen in place for at minimum 3 seconds following activation (count slowly 1, 2, 3).



Risk

These use errors could potentially delay or prevent emergency treatment of epinephrine. Since EpiPen is administered for severe and potentially life-threatening allergic reactions, anything that prevents or delays the administration of the intended dose of epinephrine could result in a high risk to the patient, including the risk of death. Additionally, failure to hold EpiPen in the correct orientation could result in inadvertent puncture of the hand, which could lead to infection, anaphylactic shock, or death. Failure to administer EpiPen in the outer thigh could result in incomplete treatment or a bone strike. Incomplete treatment could lead to worsened patient outcomes, including possibly death. Bone strike could lead to infection or nerve injury.

Important Training Reminders

- It is important that you review the Patient Information and Instructions for Use with your patients and caregivers at the time of prescribing and dispensing of EpiPen, as well as during your regular patient interactions.
- It is important that you demonstrate use of the EpiPen with your patients and caregivers. During this review and demonstration reinforce the correct administration associated with the use errors in the above chart.
- In addition, encourage patients and their caregivers to regularly read and to ensure they understand the Patient Information and Instructions for Use.
- Please refer to Appendix 2 of this letter for the Patient Information and Instructions For Use.
- The complete Prescribing Information can be found at <https://www.epipen.com/>.
- Patients and caregivers should periodically practice using the EpiPen trainer, a needle-less, non-drug containing device, referred to as the Trainer in this letter, and included in the EpiPen carton.
- Healthcare providers and consumers should review training resources on EpiPen's Instructions For Use on a regular basis, which can be found on the product website at <https://www.epipen.com/about-epipen-and-generic/how-to-use-epipen>, as well as the official EpiPen YouTube channel at <https://www.youtube.com/user/EpiPenOfficial>.

AFFECTED PRODUCT

- EpiPen® 0.3 mg (EpiPen® NDC 49502-500-02) (Authorized Generic NDC 49502-102-02)
- EpiPen Jr® 0.15 mg (EpiPen Jr® NDC 49502-501-02) (Authorized Generic NDC 49502-101-02)

CONTACT AND REPORTING INFORMATION

Please contact Mylan Customer Relations at 1-800-796-9526 (Monday-Friday 8 a.m. - 5 p.m. ET) for any questions you may have regarding this notification.

To report adverse reactions or quality issues, contact Mylan at 1-877-4-INFO-RX (1-877-446-3679).

Adverse events or quality problems experienced with the use of this product may be reported to the FDA's MedWatch Adverse Event Reporting Program either online, by regular mail, phone, or by fax:

- Complete and submit the report Online: www.fda.gov/medwatch/report.htm
- Regular mail, phone, or Fax: download form www.fda.gov/MedWatch/getforms.htm or call 1-800-332-1088 to request a reporting form, then complete and return to the address on the pre-addressed form, or submit by fax to 1-800-FDA-0178 (1-800-332-0178)



This letter is not intended as a complete description of the benefits and risks related to the use of EpiPen® 0.3 mg and EpiPen Jr® 0.15 mg Auto-Injectors, and the authorized generic versions of these strengths. Full Prescribing Information is available at <https://www.epipen.com/>.

We understand the challenge and inconvenience that the additional actions requested in this letter and in Appendix 1 may pose. Thank you for your attention to these important reminders and continued training to patients and caregivers to ensure proper use and reporting of any potential concerns or questions regarding their EpiPen.

Sincerely,

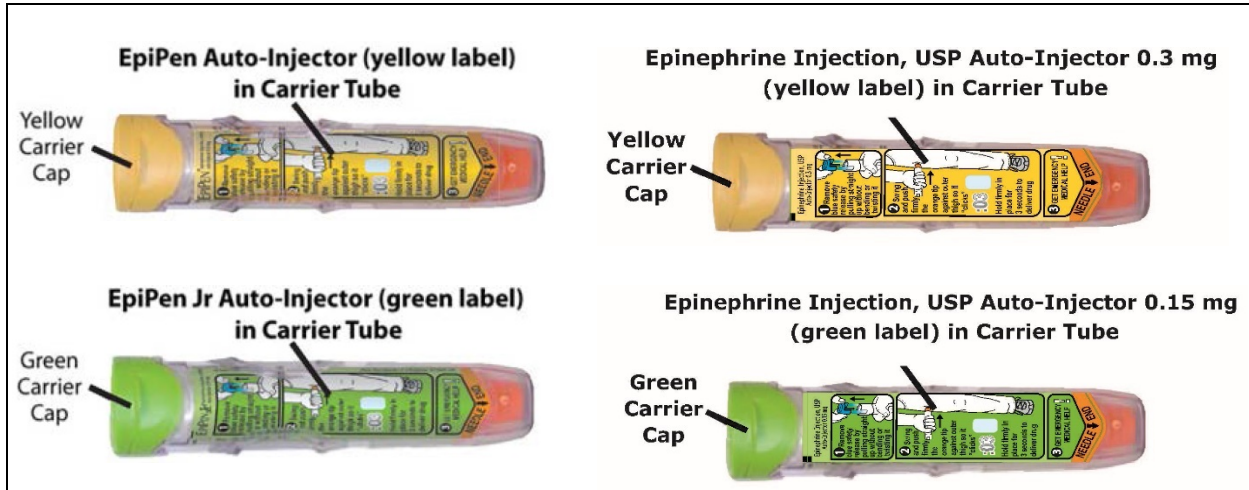
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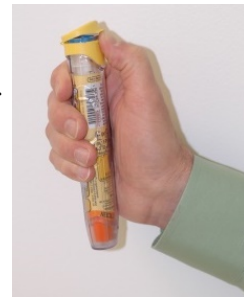
Appendix 1: Precautionary Handling Instructions for Healthcare Providers and Consumers Verifying EpiPen® Auto-Injectors for Ease of Removal from Carrier Tube and No Raised Blue Safety Release

EpiPen® 0.3 mg and EpiPen Jr® 0.15 mg Auto-Injectors, and the authorized generic versions of these strengths, inside the carrier tubes are shown below in Figure 1.

Figure 1. Auto-Injectors in the Carrier Tubes



1. Before dispensing or administering EpiPen 0.3 mg and EpiPen Jr 0.15 mg Auto-Injectors, and the authorized generic versions of these strengths, open the carton and remove both carrier tubes containing auto-injectors from the carton. Leave all other contents inside the carton (i.e., package inserts and auto-injector trainer).
2. Remove both carrier tubes from the S-clip.
3. Per the Instructions for Use, flip open the caps of the carrier tubes. The carrier tube caps are:
 - a. yellow for EpiPen or Epinephrine 0.3 mg, and
 - b. green for EpiPen Jr or Epinephrine 0.15 mg.



4. Tip each carrier tube and verify that each auto-injector readily slides out of the tube.



5. Visually inspect both auto-injectors to confirm the blue safety release is not raised: (Note: Quarter is included for thickness reference only.)



Call Mylan to obtain a replacement unit(s) at no additional cost.



OK to dispense or use.

If the blue safety release is raised, return EpiPen to the carrier tube, close the carrier tube lid and return the unit. Do *NOT* attempt to push the blue safety release back down.

The blue safety release should be kept on the auto-injector until the time of use. Do *NOT* remove the blue safety release from the auto-injector unless you are ready to use the auto-injector.

6. If both auto-injectors readily slide from the carrier tube *AND* the blue safety release is not raised:
 - a. place both auto-injectors back into the carrier tubes,
 - b. close both carrier tube caps,
 - c. connect both carrier tubes to the S-clip, and
 - d. place both auto-injectors back into the carton.

Ensure all contents (both carrier tubes each containing an auto-injector, S-clip connecting the carrier tubes, package inserts and auto-injector trainer) are placed back inside the carton and close the carton. These auto-injectors are ready to be dispensed or used.

7. If an auto-injector does not readily slide out of the carrier tube *OR* if the blue safety release is raised, the auto-injector should *NOT* be dispensed or used. Contact Mylan Customer Relations at 1-800-796-9526 to obtain a replacement unit(s) at no additional cost.



Appendix 2: Patient Information and Instructions for Use

Instructions for Use

EPIPEN®

(epinephrine injection, USP) Auto-Injector 0.3 mg

EpiPen® = one dose of 0.3 mg epinephrine, USP 0.3 mg/0.3 mL

EPIPEN JR®

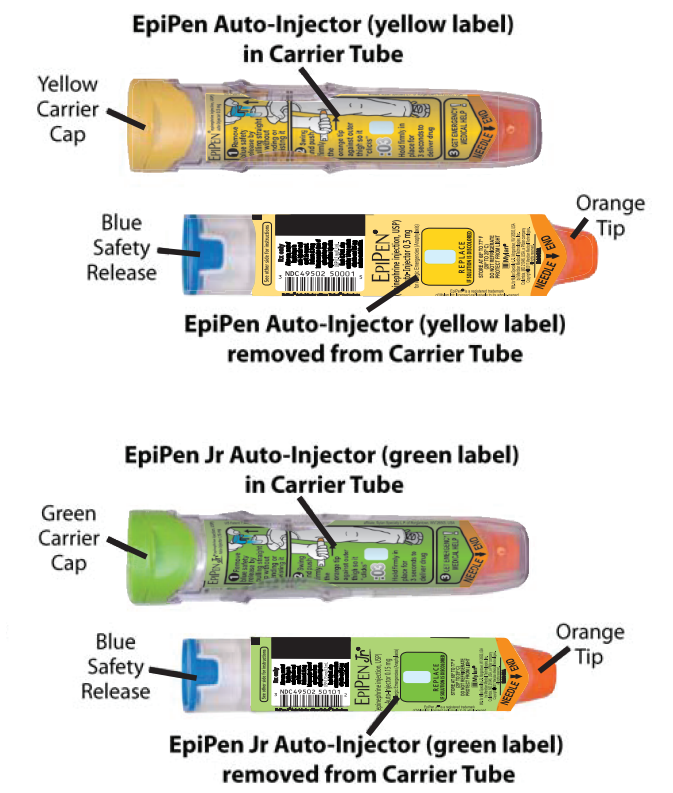
(epinephrine injection, USP) Auto-Injector 0.15 mg

EpiPen Jr® = one dose of 0.15 mg epinephrine, USP 0.15 mg/0.3 mL

For allergic emergencies (anaphylaxis)

Read these Instructions for Use carefully before you use EpiPen or EpiPen Jr. Before you need to use your EpiPen or EpiPen Jr, make sure your healthcare provider shows you the right way to use it. Parents, caregivers, and others who may be in a position to administer EpiPen or EpiPen Jr Auto-Injector should also understand how to use it as well. If you have any questions, ask your healthcare provider.

Your EpiPen and EpiPen Jr Auto-Injector



A dose of EpiPen or EpiPen Jr requires 3 simple steps: Prepare, Administer and Get emergency medical help

Step 1. Prepare EpiPen or EpiPen Jr for injection

Remove the EpiPen or EpiPen Jr from the clear carrier tube.



Flip open the yellow cap of your EpiPen or the green cap of your EpiPen Jr carrier tube.



Tip and slide the auto-injector out of the carrier tube.



Grasp the auto-injector in your fist with the orange tip (needle end) pointing downward.

With your other hand, remove the blue safety release by pulling straight up without bending or twisting it.

Note:

- The needle comes out of the orange tip.
- To avoid an accidental injection, never put your thumb, fingers or hand over the orange tip. If an accidental injection happens, get medical help right away.

Step 2. Administer EpiPen or EpiPen Jr

If you are administering EpiPen or EpiPen Jr to a young child, hold the leg firmly in place while administering an injection.



Place the orange tip against the middle of the outer thigh (upper leg) at a right angle (perpendicular) to the thigh.

Swing and push the auto-injector firmly until it 'clicks'. The click signals that the injection has started.



Hold firmly in place for 3 seconds (count slowly 1,2,3). The injection is now complete.



Remove the auto-injector from the thigh. The orange tip will extend to cover the needle. If the needle is still visible, do not attempt to reuse it.



Massage the injection area for 10 seconds.

Step 3. Get emergency medical help now.

You may need further medical attention. You may need to use a second EpiPen or EpiPen Jr Auto-Injector if symptoms continue or recur.

- Take your used auto-injector with you when you go to see a healthcare provider.
- Tell the healthcare provider that you have received an injection of epinephrine. Show the healthcare provider where you received the injection.
- Give your used EpiPen or EpiPen Jr Auto-Injector to the healthcare provider for inspection and proper disposal.
- Ask for a refill, if needed.

Note:

- The used auto-injector with extended needle cover will not fit in the carrier tube.
- EpiPen and EpiPen Jr are single-use injectable devices that deliver a fixed dose of epinephrine. The auto-injector cannot be reused. Do not attempt to reuse EpiPen after the device has been activated. It is normal for most of the medicine to remain in the auto-injector after the dose is injected. The correct dose has been administered if the orange needle tip is extended and the window is blocked.
- Your EpiPen and EpiPen Jr Auto-Injector may come packaged with an EpiPen Trainer and separate Trainer Instructions for Use. The EpiPen Trainer has a grey color. The grey EpiPen Trainer contains no medicine and no needle. Practice with your EpiPen Trainer, but always carry your real EpiPen or EpiPen Jr Auto-Injector in case of an allergic emergency.
- If you will be administering EpiPen or EpiPen Jr to a young child, ask your healthcare provider to show you how to properly hold the leg in place while administering a dose.
- Do not try to take the EpiPen or EpiPen Jr Auto-Injector apart.

This Patient Information and Instructions for Use has been approved by the U.S. Food and Drug Administration.

Manufactured for:

Mylan Specialty L.P., Morgantown, WV 26505, U.S.A. by Meridian Medical Technologies, Inc., Columbia, MD 21046, U.S.A., a Pfizer company

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MS:PIL:EPI:R3
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EPIPEN®

(epinephrine injection, USP) Auto-Injector 0.3 mg

EpiPen® = one dose of 0.3 mg epinephrine, USP 0.3 mg/0.3 mL

EPIPEN JR®

(epinephrine injection, USP) Auto-Injector 0.15 mg

EpiPen Jr® = one dose of 0.15 mg epinephrine, USP 0.15 mg/0.3 mL

MyEpiPen.com

Register your EpiPen or EpiPen Jr Auto-Injector at **MyEpiPen.com** and find out more about:

- Free EpiPen Auto-Injector **Refill Reminder Program**. It is important to keep your auto-injector up-to-date.

Register up to 6 EpiPen or EpiPen Jr Auto-Injectors and receive automatic **Refill Reminder Alerts**.

- Receive periodic information related to allergies and allergens.
- Instructional Video

For more information about EpiPen or EpiPen Jr Auto-Injectors and proper use of the product, call Mylan at 1-877-446-3679 or visit www.epipen.com.