FDA Drug Safety Communication

FDA adds Boxed Warning about a rare but serious allergic reaction called anaphylaxis with the multiple sclerosis medicine glatiramer acetate (Copaxone, Glatopa)

Treat immediately if symptoms worsen or do not go away shortly after an injection

01-22-2025 FDA Drug Safety Communication

What safety concern is FDA announcing?

The U.S. Food and Drug Administration (FDA) is warning about the risk of a rare but serious allergic reaction with the medicine glatiramer acetate (Copaxone, Glatopa), which is used to treat patients with multiple sclerosis (MS). This serious allergic reaction, called anaphylaxis, can occur at any time while on treatment, after the first dose or after doses administered months or years after starting the medicine. For most patients who experienced anaphylaxis with glatiramer acetate use, the symptoms appeared within one hour of injection. In some cases, anaphylaxis resulted in hospitalization and death.

The initial symptoms of anaphylaxis can overlap with those of a common reaction called immediate post-injection reaction that is temporary and can start soon after a shot is given. While immediate post-injection reaction is common, anaphylaxis is rare and its symptoms are typically more severe, worsen over time, and require treatment. Patients experiencing a reaction after the medicine is administered should seek immediate medical attention if the symptoms are more than mild, get worse over time, or do not go away within a brief time. We are adding a new *Boxed Warning* about this risk to the glatiramer acetate prescribing information and patient Medication Guide.

What is FDA doing?

We are adding the risk of anaphylaxis to a new *Boxed Warning*, FDA's most prominent warning, and to the *Warnings and Precautions* section of the glatiramer acetate prescribing information. These warnings include information that anaphylaxis can occur at any time, from as early as after the first dose or after doses administered years after starting the medicine. We are also adding new recommendations for patients and health care professionals about the critical importance of quickly recognizing and treating symptoms of anaphylaxis. The updated prescribing information also instructs patients to stop taking the medicine and seek immediate medical attention by going to an emergency room or calling 911 if symptoms of anaphylaxis occur.

What is glatiramer acetate (Copaxone, Glatopa) and how can it help me?

Glatiramer acetate is an FDA-approved medicine to treat patients with relapsing forms of MS. It works by lessening the immune system's abnormal attack on nerves in the brain and spinal cord. This medicine helps decrease the number of MS relapses. Glatiramer acetate is available as an injectable medicine administered daily or three times per week, depending on dosage, under the brand name Copaxone, branded generic name Glatopa, and as other generic glatiramer acetate products. The first glatiramer acetate product, Copaxone, was approved in 1996.

What should patients and caregivers do?

Patients should stop taking glatiramer acetate and seek immediate medical attention by going to an emergency room or calling 911 if you experience symptoms of an anaphylactic reaction. Symptoms generally appear within one hour of injection and include wheezing or difficulty breathing, swelling of

the face, lips, or throat, and hives. These symptoms can quickly progress to more serious symptoms, including severe rash or shock, which is a life-threatening condition. Anaphylaxis can occur at any point during glatiramer acetate treatment, including years after starting treatment. You should not restart glatiramer acetate if you have experienced anaphylaxis unless another clear cause for anaphylaxis is identified. Talk to your health care professional if you have any questions or concerns about glatiramer acetate.

Patients should be aware that the early symptoms of anaphylaxis can be similar to a temporary reaction that sometimes happens right after or within minutes after an injection of the medicine into the skin. This immediate post-injection reaction goes away on its own, usually within 15-30 minutes, with no specific treatment. This reaction can occur with the first dose, or after doses administered months or even years after starting the medicine. This immediate post-injection reaction may involve symptoms such as flushing, chest pain, palpitations, anxiety, shortness of breath, rash, or hives. Call the health care professional who prescribed the medicine if you have any of these immediate post-injection reaction symptoms. Do not continue taking more injections until your prescriber tells you to do so. Seek immediate medical attention by going to an emergency room or calling 911 if any of these symptoms worsen or do not go away.

What should health care professionals do?

Health care professionals should be aware that fatal anaphylaxis has occurred with glatiramer acetate, including years after treatment has been initiated and that the symptoms of these rare anaphylactic events may overlap with those of common immediate post-injection reactions. Symptoms such as flushing, chest pain, palpitations, anxiety, shortness of breath, rash, or hives typically occur within minutes after an injection and are generally transient, self-limited, and resolve without specific treatment within 30 minutes. Those associated with anaphylaxis are typically more severe, worsen, or last longer, requiring urgent medical attention.

Educate patients on the signs and symptoms of anaphylaxis and immediate post-injection reactions. Instruct them to seek immediate medical attention by going to an emergency room or calling 911 if they experience any symptoms of anaphylaxis, and to contact their prescriber if they experience an immediate post-injection reaction. Do not restart the medicine in patients who experience anaphylaxis unless a clear alternative etiology is identified.

What did FDA find?

We identified 82 worldwide cases of anaphylaxis associated with glatiramer acetate occurring from December 1996 through May 2024, including 19 cases that reported anaphylaxis more than one year after starting the medicine (see Data Summary). The 82 worldwide cases include only reports submitted to FDA* and found in the medical literature so there are likely additional cases about which we are unaware. While anaphylaxis in these cases appears to be rare compared to how often the medicine is used (see Facts about Glatiramer Acetate), these 82 patients reported serious outcomes that required emergency room visits or hospitalizations for medical treatment, and six died. A majority of the 82 patients experienced anaphylaxis within one hour of taking the medicine.

*The cases were reported to the FDA Adverse Event Reporting System (FAERS) database.

What is my risk?

All medicines have side effects even when used correctly as prescribed. It is important to know that people respond differently to all medicines depending on their health, the diseases they have, genetic factors, other medicines they are taking, and many other factors. As a result, we cannot determine how likely it is that someone will experience these side effects when taking glatiramer acetate. Your health care professionals know you best, so talk to them if you have questions or concerns about risks of taking glatiramer acetate.

How do I report side effects from glatiramer acetate (Copaxone, Glatopa)?
To help FDA track safety issues with medicines, we urge patients and health care professionals to report side effects involving glatiramer acetate or other medicines to the FDA MedWatch program using the information in the "Contact FDA" box at the bottom of this page.

How can I get new safety information on medicines I'm prescribing or taking?
You can sign up for email alerts about Drug Safety Communications on medicines or medical specialties of interest to you.

Facts about Glatiramer Acetate (Copaxone, Glatopa)

- Glatiramer acetate is a prescription medicine approved by FDA to reduce the frequency of relapses in patients with multiple sclerosis (MS).
- Glatiramer acetate works by lessening the immune system's abnormal attack on nerves in the brain and spinal cord. This helps decrease the number of MS relapses.
- Glatiramer acetate is given as an injection under the skin and should be taken according to the prescribed dosing schedule to be effective.
- Common side effects that may occur seconds to minutes after injection, called immediate post-injection reactions, include flushing, rash, short-term difficulty breathing, and chest pain. These may overlap with signs and symptoms associated with the rare but serious anaphylaxis allergic reactions.
- In 2023, an estimated 240,000 glatiramer acetate prescriptions were dispensed and estimated 32,000 patients received a dispensed prescription from U.S. outpatient retail and mail order pharmacies.[1]

Additional Information for Patients and Caregivers

- FDA is warning that a rare but potentially life-threatening allergic reaction has been reported with the multiple sclerosis (MS) medicine glatiramer acetate. This serious allergic reaction, called anaphylaxis, can occur after the first dose or after doses administered months or even years after starting treatment. It can result in hospitalization and death.
- Initial symptoms of anaphylaxis may overlap with reactions that can happen shortly after an injection of the medicine into the skin, called immediate post-injection reactions. This could lead to a delay in recognizing and treating anaphylaxis, which can be life-threatening.
- If you experience symptoms of anaphylaxis, stop taking glatiramer acetate and seek immediate medical attention by going to an emergency room or calling 911. These symptoms include:
    - wheezing or difficulty breathing
    - swelling of the face, lips, or throat
    - hives
    - severe rash

- Immediate post-injection reactions, in contrast, are common, temporary reactions that usually go away within 15-30 minutes without lasting effects. These symptoms include the following, but if any of them get worse or persist, immediate medical attention may be necessary:
    - flushing or warmth
    - chest pain
    - fast heartbeat
    - anxiety
    - breathing problems or tightness in your throat
    - swelling, rash, hives, or itching
- Be aware that immediate post-injection reactions are common, typically happen right after or within minutes after injection, and go away quickly, while anaphylactic reactions are rare, generally occur within one hour of an injection, and the symptoms are typically more severe, do not go away, get worse, and require treatment. Both reactions can occur after the first injection or after injections administered any time while on treatment, even after an injection given several years into treatment. However, anaphylaxis is a medical emergency needing immediate treatment.
- If you have had symptoms of anaphylaxis or an immediate post-injection reaction, do not give yourself more injections until your prescriber tells you to do so.
- Talk to your prescriber if you have any questions or concerns about glatiramer acetate.
- Read the patient Medication Guide that comes with your prescription because there may be new or important additional information about the medicine. The patient information leaflet explains the important things you need to know about the medicine. These include the side effects, what the medicine is used for, how to take and store it properly, and other things to watch out for when you are taking the medicine.
- To help FDA track safety issues with medicines, report side effects from glatiramer acetate or other medicines to the FDA MedWatch program using the information in the "Contact FDA" box at the bottom of this page.
- You can sign up for email alerts about Drug Safety Communications on medicines and medical specialties of interest to you.

Additional Information for Health Care Professionals

- FDA is warning that cases of life-threatening anaphylaxis have been reported with multiple sclerosis medicine glatiramer acetate, resulting in hospitalization and death. This reaction can occur after the first dose or after injections administered any time while on treatment, even after an injection given several years after starting the medicine. In most of the reported cases, anaphylaxis occurred within an hour of administering the medicine.
- We are adding the risk of anaphylaxis and recommendations for patients and health care professionals to a new *Boxed Warning*, FDA's most prominent warning, and to the *Warnings and Precautions* section of the glatiramer acetate prescribing information.
- Be aware that initial symptoms of anaphylaxis might overlap with those of an immediate post-injection reaction, which could lead to a delay in recognizing and treating anaphylaxis.
- Educate patients on the signs and symptoms of immediate post-injection reactions, which are common, typically occur within minutes after the injection, and can involve symptoms such as flushing, chest pain, palpitations, anxiety, shortness of breath, rash, or hives. These symptoms are generally transient and resolve without specific treatment within 30 minutes. .Instruct them

to contact their prescriber if they experience any of these symptoms and discontinue taking the medicine until instructed to restart.

- Explain the signs and symptoms of anaphylaxis and instruct patients to stop taking glatiramer acetate and seek immediate medical attention by going to an emergency room or calling 911 if they develop these symptoms.
- Do not restart the medicine in patients that experience anaphylaxis unless a clear alternative etiology is identified.
- Encourage patients to read the patient Medication Guide that comes with their prescription because there may be new or important additional information about the medicine.
- To help FDA track safety issues with medicines, report adverse events involving glatiramer acetate or other medicines to the FDA MedWatch program using the information in the "Contact FDA" box at the bottom of this page.
- You can sign up for email alerts about Drug Safety Communications on medicines and medical specialties of interest to you.

Data Summary

FDA reviewed 82 serious cases of anaphylaxis worldwide associated with glatiramer acetate in the FAERS database and medical literature[2-8] since the product was approved in December 1996 through May 2024. Of the 82 patients, 51 were hospitalized for anaphylaxis, including 13 who required care in the intensive care unit, and six died. Most of these reactions occurred within one hour of injection. The median time to onset of anaphylaxis from starting glatiramer acetate was 5 months, ranging from one day to 72 months as follows: 12 patients within one month of starting the medicine, 48 patients between one and 12 months after starting, and 19 patients more than 12 months after starting it. One patient case described shock and sudden death after the first dose, and the duration of treatment was not reported for three patients. Treatments reported in patients who experienced anaphylaxis included epinephrine or adrenaline (n=32), corticosteroids (n=21), mechanical ventilation (n=5), and cardiopulmonary resuscitation (n=1). For context, there are more than 3 million patient-years of exposure to glatiramer acetate in the postmarket setting from 1996 through 2023.

References

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