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5/8/2025

IMPORTANT DRUG WARNING

Subject: **Serious Risk of Anaphylactic Reactions in Patients taking COPAXONE® (glatiramer acetate injection)**

Dear Healthcare Provider:

Teva Pharmaceuticals USA, Inc. in agreement with the U.S. Food and Drug Administration (FDA) would like to inform you of the revised labeling for COPAXONE® (glatiramer acetate injection) for subcutaneous use regarding the risk of anaphylactic reactions with use of COPAXONE. The prescribing information has been revised to include a new boxed warning, a new section 5.1 – Anaphylactic Reactions, and updates to section 5.2 – Immediate Post-Injection Reaction.

In addition, the Patient Counseling Information has been updated accordingly, and the Patient Leaflet was converted to a Medication Guide.

Summarized below are the revisions to the label:

WARNING: ANAPHYLACTIC REACTIONS

Cases of life-threatening and fatal anaphylaxis have been reported with COPAXONE. Anaphylaxis can occur at any time following initiation of therapy, from as early as after the first dose, up to years following initiation of therapy.

- **Make patients aware of the symptoms of anaphylaxis, which may overlap with those of an immediate post-injection reaction; instruct them to seek immediate medical care should these symptoms occur. Prompt identification of anaphylaxis is important to avoid a delay in treatment *[see Warnings and Precautions (5.1)].***

- **COPAXONE is contraindicated in patients with a history of hypersensitivity reactions to COPAXONE, including anaphylaxis. If an anaphylactic reaction occurs, treatment with COPAXONE must be immediately discontinued. Unless a clear alternative etiology is identified, COPAXONE must be permanently discontinued *[see Contraindications (4) and Warnings and Precautions (5.1)].***

WARNINGS AND PRECAUTIONS

Anaphylactic Reactions (5.1)

Life-threatening and fatal anaphylaxis has been reported with COPAXONE *[see Adverse Reactions (6.2)]*. COPAXONE is contraindicated in patients with a history of hypersensitivity reactions to COPAXONE, including anaphylaxis *[see Contraindications (4)]*. Anaphylaxis can occur at any time following initiation of COPAXONE therapy, from as early as after the first dose, up to years after initiation of treatment. Anaphylaxis occurred within an hour of a COPAXONE injection in most of the reported cases.

Some signs and symptoms of anaphylactic reactions may overlap with those of immediate post-injection reactions *[see Warnings and Precautions (5.2)]*. All patients receiving treatment with COPAXONE and caregivers should be informed about the signs and symptoms of anaphylactic reactions, and that they must seek immediate emergency medical care in case of experiencing such symptoms. If an anaphylactic reaction occurs, treatment with COPAXONE must be immediately discontinued. Unless a clear alternative etiology is identified, COPAXONE must be permanently discontinued *[see Contraindications (4)]*.

Immediate Post-Injection Reaction (5.2)

Approximately 16% of patients exposed to COPAXONE 20 mg per mL in the 5 placebo-controlled trials compared to 4% of those on placebo, and approximately 2% of patients exposed to COPAXONE 40 mg per mL in a placebo-controlled trial compared to none on placebo, experienced a constellation of symptoms that may occur immediately (within seconds to minutes, with the majority of symptoms observed within 1 hour) after injection and included at least two of the following: flushing, chest pain, palpitations, tachycardia, anxiety, dyspnea, constriction of the throat, and urticaria. These events are termed immediate post-injection reactions.

The symptoms of an immediate post-injection reaction may overlap with those of anaphylaxis; prompt identification of anaphylaxis is important to avoid a delay in treatment. In general, symptoms of an immediate post-injection reaction have onset several months after the initiation of treatment, although they may occur earlier, and a given patient may experience one or several episodes of these symptoms. Whether or not any of these symptoms actually represent a specific syndrome is uncertain. Typically, the symptoms are transient and self-limited and do not require treatment; however, there have been reports of patients with similar symptoms who developed fatal anaphylaxis and/or received emergency medical care. Whether an immunologic or nonimmunologic mechanism mediates these episodes, or whether several similar episodes seen in a given patient have identical mechanisms, is unknown.

Prescriber Action

As noted in the *Patient Counseling Information* section (17), advise patients and their caregivers that COPAXONE may cause life-threatening and fatal anaphylactic reactions shortly after injection, and that reactions may occur from as early as after the first dose, up to years after initiation of treatment.

- Advise patients to read the new Medication Guide for more information.
- Inform patients and their caregivers about the signs and symptoms specific for anaphylactic reactions, and that signs and symptoms of anaphylactic reactions may overlap with those of immediate post-injection reactions, which occur within seconds to minutes after injection and are generally transient, self-limited, and do not require specific treatment.
- Instruct patients to seek immediate emergency medical care if they experience any signs or symptoms of an anaphylactic reaction, or if symptoms of a potential immediate post-injection reaction are more than mild, get worse over time, or do not go away within a brief time.
- Instruct patients to contact their healthcare provider if they experience signs or symptoms of an immediate post-injection reaction such as flushing, chest pain, palpitations, anxiety, shortness of breath, rash, or hives.
- Patients should also be advised to contact their healthcare provider, and that treatment should be discontinued immediately and permanently, if anaphylactic reactions occur.

Reporting Adverse Events

Healthcare providers and patients are encouraged to report adverse events in patients taking COPAXONE to Teva Pharmaceuticals at 1-888-483-8279. Adverse events or quality problems experienced with the use of this product may also be reported to the FDA's MedWatch Adverse Event Reporting Program either online, or regular mail, or by fax:

- Complete and submit the report **Online**: www.fda.gov/medwatch/report.htm
- **Regular mail 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.

You also may contact our medical information department at 1-888-483-8279 if you have any questions about the information contained in this letter or the safe and effective use of COPAXONE.

Sincerely,

Denisa Hurtukova, MD
Vice President, Head of U.S. Medical Affairs
Teva Pharmaceuticals USA, Inc.

Enclosure(s): Full Prescribing Information for COPAXONE® (glatiramer acetate injection), for subcutaneous use.