Healthy Skin Practices
Caring for your skin throughout your COPAXONE® (glatiramer acetate injection) therapy

Bill S., diagnosed with a relapsing form of MS
The Importance of Healthy Skin

People on injectable therapies, including Teva's COPAXONE® (glatiramer acetate injection), can develop skin reactions known as injection site reactions (ISRs). Therefore, it's very important to inject properly and keep your skin in good condition.

This guide provides helpful tips and recommendations to help keep your skin healthy and manage ISRs. Taking steps to maintain healthy skin can help you stay committed to your relapsing MS treatment.

A permanent indentation under the skin (lipoatrophy or, rarely, necrosis) at the injection site may occur, due to local destruction of fat tissue. Be sure to follow proper injection technique and inform your doctor of any skin changes.

Use

COPAXONE® is a prescription medicine that is used to treat relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

Important Safety Information

Do not use COPAXONE® if you are allergic to glatiramer acetate or mannitol.

Please see Important Safety Information on Page 11, and read the Patient Information in the accompanying full Prescribing Information.

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Teva’s Shared Solutions® provides training and tools to help maintain the health of your skin, and help you gain the confidence to manage your injection routine.
Understanding Your Skin

Your skin, the largest and most visible organ in your body, has many important functions. The three main layers of the skin—the epidermis, dermis, and subcutaneous layer—each have specific roles.

1. **Epidermis**: the outermost layer that is constantly shed and regenerated.³
   - Contains melanin, which protects you from harmful ultraviolet (UV) rays.³
   - Contains keratin, a protein cell that gives the skin its toughness.⁵
   - Protects you from most bacteria, viruses, and other foreign substances.³
   - Protects the internal organs, muscles, nerves, and blood vessels.³

2. **Dermis**: the thick elastic inner layer.³
   - Gives the skin strength and flexibility (collagen and elastin).
   - Contains nerve endings, blood vessels, hair follicles, and sweat and oil glands.
   - Blood vessels and hair follicles in the dermis help regulate body temperature.
   - Senses touch, heat, cold, and pain.

3. **Subcutaneous layer**: the deepest layer of skin, which is mostly composed of fatty tissue where COPAXONE® is injected.²
   - Contains blood vessels and nerves.
   - Provides a cushion to protect the body from injuries.
   - Helps insulate the body from extreme heat and cold.

COPAXONE® (glatiramer acetate injection) is for subcutaneous injection only.

Please see Important Safety Information on Page 11, and read the Patient Information in the accompanying full Prescribing Information.
**General Tips For Healthy Skin**

Proper skin care is important for everyone, including relapsing multiple sclerosis (RMS) patients using injectable therapies like COPAXONE® (glatiramer acetate injection). There are many ways to help keep your skin as healthy as possible.

**Always protect your skin, regardless of the weather**

- Bask in the shade rather than in the sun—heat or high humidity can cause many people with RMS to experience a temporary worsening of their symptoms.\(^6\)
- Use moisturizers and sunblock with UV protection whenever you plan on being outdoors, even on cloudy days.
- Wear lightweight clothing to allow your skin to breathe.

**Be gentle to your skin**\(^7\)

- Hot water and long baths or showers deplete your skin of natural oils.
  - Limit bath or shower time.
  - Warm water is preferable to hot water.
- Gently pat your skin dry after bathing so that some moisture remains on your skin.
- Avoid strong soaps and detergents.
- Be careful when you shave. Use shaving cream, lotion, or gel to moisturize your skin.

**Don't smoke**\(^7\)

- Smoking can result in loss of oxygen and nutrients in the skin.
- Smoking can also damage collagen and elastin, causing your skin to lose strength and elasticity.

**Maintain a healthy dietary pattern that includes**\(^8,9\):

- A variety of fruits and vegetables.
- Whole grains.
- Low-fat dairy products.
- Skinless poultry and fish.
- Nuts and beans.
- Non-tropical vegetable oils (eg, canola, corn, olive oils, etc.).

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Please see Important Safety Information on Page 11, and read the Patient Information in the accompanying full Prescribing Information.
Helpful Injection Tips for COPAXONE®
(glatiramer acetate injection)

1 Ready to begin? Take the COPAXONE® Pre-filled Syringe out of the refrigerator at least 20 minutes before you inject.1 Injecting when COPAXONE® is at room temperature can help you avoid discomfort.

2 Apply a warm compress to the injection site (with a cloth barrier between the warm compress and bare skin) for 5 minutes to help relax the tissue before cleaning the site and injecting.

You should receive your first dose of COPAXONE® with a doctor or nurse present. This might be at your doctor’s office or with a visiting home health nurse who will teach you how to give your COPAXONE® injections.

3 Next, be sure to follow proper injection technique. See the step-by-step instruction video on COPAXONE.com or refer to the Instructions for Use in the accompanying full Prescribing Information.

4 After the injection, use a cold pack (with a cloth barrier between the cold pack and bare skin) on the injection site for up to 1 minute.

The autoject® 2 for glass syringe can be a helpful tool. This automatic injection device hides the needle, allowing you to administer COPAXONE® at the touch of a button. And it’s available free of charge to anyone taking Teva’s COPAXONE® with a doctor’s prescription. Order yours through Teva’s Shared Solutions® at 1-800-887-8100 or visit COPAXONE.com to learn more.

Please see Important Safety Information on Page 11, and read the Patient Information in the accompanying full Prescribing Information.
Injection Site Rotation

Rotation matters

Choose a different injection area on each injection day. Never inject into the same place (site) more than once a week.

- Rotate the 7 injection areas (see diagram at right) and the multiple sites within those areas.
- Avoid injecting in the same site over and over again.

Since every body type is different, talk with your doctor about the injection areas that are best for you.

The COPAXONE iTracker® 2.0 mobile app for iPhone® and Android™ can assist with injection site rotation, injection logging, reminders, and other tools. Visit COPAXONE.com for more information.

Please see Important Safety Information on Page 11, and read the Patient Information in the accompanying full Prescribing Information.
Teva's Shared Solutions® 1-on-1 Injection Training

When beginning Teva’s COPAXONE® (glatiramer acetate injection), small adjustments to your injection technique or schedule may positively impact your injection experience.

Teva’s Shared Solutions® provides personalized, in-home, 1-on-1 injection training to COPAXONE® patients. Your session is provided at no cost and can be as short or long as you require.

During your session, Teva-trained nurses can:

- Educate you on tips and tools to help maintain skin health.
- Provide new tips and techniques to help make your injection experience more comfortable and convenient.
- Ensure you are rotating injection sites properly.
- Educate you about the latest injection management tools, including the COPAXONE iTracker® 2.0 mobile app for Apple® and Android™.

You can also find video injection tutorials and other helpful injection tips online at COPAXONE.com.

Everyone’s injection experience is different. It’s important to make it work for you so you can stay committed to therapy. Be sure to discuss your injection routine and any questions you may have with your doctor. Always follow your doctor’s recommendations.

Call Teva's Shared Solutions® at 1-800-887-8100 to set up a free, in-home, 1-on-1 injection training session.

Please see Important Safety Information on Page 11, and read the Patient Information in the accompanying full Prescribing Information.
Immediate Post-Injection Reactions

Serious side effects may happen right after or within minutes after you inject COPAXONE® (glatiramer acetate injection) at any time during your course of treatment. Call your doctor right away if you have any of these immediate post-injection reaction symptoms including:

- redness to your cheeks or other parts of the body (flushing)
- chest pain
- fast heart beat
- anxiety
- breathing problems or tightness in your throat
- swelling, rash, hives, or itching

If you have symptoms of an immediate post-injection reaction, do not give yourself more injections until a doctor tells you to.

You can have chest pain as part of an immediate post-injection reaction or by itself. This type of chest pain usually lasts a few minutes and can begin around 1 month after you start using COPAXONE®. Call your doctor right away if you have chest pain while using COPAXONE®.

Lipoatrophy

Damage to the fatty tissue just under your skin’s surface (lipoatrophy) and, rarely, death of your skin tissue (necrosis) can happen when you use COPAXONE®. This can cause a “dent” at the injection site that may not go away.

Tips. Always talk to your doctor about these tips and other ways to help manage your injection routine.

- Rotate injection areas and sites regularly.
- Do not inject in or near sites where the skin has scarring or “dents.”
- Talk to an MS-certified nurse by phone at 1-800-887-8100 if you have questions or concerns.
Common Injection Site Reactions

The tips in this section can help you manage some of the common side effects impacting the skin, also called injection site reactions (ISRs), associated with COPAXONE® (glatiramer acetate injection).1

Some of the ISRs described in this section could also be a symptom of an Immediate Post-Injection Reaction discussed on the previous page. Always talk to your doctor about any symptoms you may experience.

Redness1,10
Characterized by redness of the skin due to inflammation and may involve dilated or congested capillaries. Skin color can range from bright red in patients with acute conditions to pale violet or brown in those with chronic problems.

Tips. Always talk to your doctor about these tips and other ways to help manage your injection routine.10

Examine the injection site carefully before injection.

Avoid injecting in damaged areas.

Do not rub the injection site after injecting.

Pain1,10
Pain at or near the injection site may be a side effect that commonly occurs for patients receiving injectable therapies.

Redness1,10
Characterized by redness of the skin due to inflammation and may involve dilated or congested capillaries. Skin color can range from bright red in patients with acute conditions to pale violet or brown in those with chronic problems.

Tips. Always talk to your doctor about these tips and other ways to help manage your injection routine.10

Examine the injection site carefully before injection.

Avoid injecting in damaged areas.

Before injecting, it may be helpful to apply a warm compress to the injection site for 5 minutes.
Common Injection Site Reactions

Inflammation or swelling\textsuperscript{1,10}
Swelling or tenderness of the skin at the injection site.

Tips. Always talk to your doctor about these tips and other ways to help manage your injection routine\textsuperscript{1,10}

To prevent inflammation, the area should be sufficiently warmed before injection.

Apply a cold pack to the injection area for up to 1 minute after injection.

Lumps\textsuperscript{1,10}
A raised area at the injection site may occur.

Tips. Always talk to your doctor about these tips and other ways to help manage your injection routine\textsuperscript{1,10}

Avoid injecting in areas of damaged skin (redness, swelling, tenderness, lumps, denting, tattoo, etc.).

Following an injection, gently press your fingers over the injection site to feel for lumps, hardness, or thickening of the skin.

If the lump persists, increases in size, becomes painful or discolored, or occurs in areas other than the injection site, please contact your doctor.

Itching at the injection site\textsuperscript{1}
Itching can occur at the injection site following the injection of COPAXONE\textsuperscript{®} (glatiramer acetate injection).

Other common side effects of COPAXONE\textsuperscript{®} include flushing, rash, shortness of breath, and chest pain. These are not all of the possible side effects of COPAXONE\textsuperscript{®}. For a complete list, ask your doctor or pharmacist. Tell your doctor about any side effects you have while taking COPAXONE\textsuperscript{®}.

Please see Important Safety Information on Page 11, and read the Patient Information in the accompanying full Prescribing Information.
Use

COPAXONE® is a prescription medicine that is used to treat relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

Important Safety Information

Do not use COPAXONE® if you are allergic to glatiramer acetate or mannitol.

Serious side effects may happen right after or within minutes after you inject COPAXONE® at any time during your course of treatment. Call your doctor right away if you have any of these immediate post-injection reaction symptoms including: redness to your cheeks or other parts of the body (flushing); chest pain; fast heart beat; anxiety; breathing problems or tightness in your throat; or swelling, rash, hives, or itching. If you have symptoms of an immediate post-injection reaction, do not give yourself more injections until a doctor tells you to.

You can have chest pain as part of an immediate post-injection reaction or by itself. This type of chest pain usually lasts a few minutes and can begin around 1 month after you start using COPAXONE®. Call your doctor right away if you have chest pain while using COPAXONE®.

Damage to the fatty tissue just under your skin’s surface (lipoatrophy) and, rarely, death of your skin tissue (necrosis) can happen when you use COPAXONE®. Damage to the fatty tissue under your skin can cause a “dent” at the injection site that may not go away. You can reduce your chance of developing these problems by following your doctor’s instructions for how to use COPAXONE® and choosing a different injection area each time you use COPAXONE®.

The most common side effects of COPAXONE® include redness, pain, swelling, itching, or a lump at the injection site; rash; shortness of breath; flushing; and chest pain.

Tell your doctor if you have any side effect that bothers you or that does not go away. These are not all the possible side effects of COPAXONE®. For more information, ask your doctor or pharmacist. Call your doctor for medical advice about side effects.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Please read the Patient Information in the accompanying full Prescribing Information.


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Healthy Skin Treatment Injection Checklist

☐ Am I injecting Teva’s COPAXONE® (glatiramer acetate injection) when the syringe is at room temperature?

☐ Have I correctly adjusted my autoject®2 for glass syringe depth settings?

☐ Am I practicing proper injection techniques, such as prepping my skin for injections (eg, using a warm compress)?

☐ Am I properly tracking my rotation sites?

☐ Am I experiencing any injection-related symptoms or problems that I’d like to discuss with a Teva-trained nurse?

Please call Teva’s Shared Solutions® at 1-800-887-8100 to make an appointment for your free, in-home, 1-on-1 injection training session.

Date of next doctor’s appointment: ______________________

Date of next 1-on-1 injection training session: _____________

Notes

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CONTRAINDICATIONS

COPAXONE is contraindicated in patients with known hypersensitivity to glatiramer acetate or mannitol.

DOSE FORMS AND STRENGTHS

- Injection: 20 mg per mL in a single-dose, prefilled syringe with a white plunger.
- COPAXONE 20 mg/mL: administer once per day
- COPAXONE 40 mg/mL: three times per week
- Before use, allow the solution to warm to room temperature.

DOSE ADMINISTRATION

- Injection: 20 mg/mL in a single-dose, prefilled syringe with a white plunger.
- Injection: 40 mg/mL in a single-dose, prefilled syringe with a blue plunger.

CONTRAINdications

Known hypersensitivity to glatiramer acetate or mannitol (4)

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2 DOSAGE AND ADMINISTRATION
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*Sections or subsections omitted from the full prescribing information are not listed.

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use COPAXONE® safely and effectively. See full prescribing information for COPAXONE.

COPAXONE (glatiramer acetate injection) for subcutaneous use

Recent Major Changes

INDICATIONS AND USAGE

COPAXONE is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

DOSAGE FORMS AND STRENGTHS

- Injection: 40 mg/mL in a single-dose, prefilled syringe with a blue plunger (3)
- Before use, allow the solution to warm to room temperature (2.2)

DOSAGE FORMS AND STRENGTHS

- Injection: 20 mg/mL in a single-dose, prefilled syringe with a white plunger.
- COPAXONE 20 mg/mL per day (2.1)
- COPAXONE 40 mg/mL per day (2.1)
- For subcutaneous injection only; doses are not interchangeable (2.1)

WARNINGS AND PRECAUTIONS

Immediate Post-Injection Reaction (flushing, chest pain, palpitations, tachycardia, anxiety, dyspnea, throat constriction, and/or urticaria), may occur within seconds to minutes after injection and are generally transient and self-limiting (5.1)

Chest pain, usually transient (5.2)

Lipoatrophy and skin necrosis may occur. Instruct patients in proper injection technique and to rotate injection sites (5.3)

COPAXONE can modify immune response (5.4)

ADVERSE REACTIONS

- In controlled studies of COPAXONE 20 mg/mL, most common adverse reactions (>10% and ≥1.5 times higher than placebo) were: injection site reactions, vasodilatation, rash, dyspnea, and chest pain.
- In a controlled study of COPAXONE 40 mg/mL, most common adverse reactions (>10% and ≥1.5 times higher than placebo) were: injection site reactions.

To report SUSPECTED ADVERSE REACTIONS, contact Teva Pharmaceuticals at 1-888-483-8279 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

USE IN SPECIFIC POPULATIONS

- Nursing Mothers: It is not known if COPAXONE is excreted in human milk.
- Pediatric Use: The safety and effectiveness of COPAXONE have not been established in patients under 18 years of age.

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 7/2019

Use in Patients with Impaired Renal Function

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY

13 NONCLINICAL TOXICOLOGY

14 CLINICAL STUDIES

15 HOW SUPPLIED/STORAGE AND HANDLING

16 PATIENT COUNSELING INFORMATION

Adverse Reactions

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, constrictio of the throat, and urticaria. In general, these symptoms have their 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 were transient and self-limited and did not require treatment; however, there have been reports of patients with similar symptoms who 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.

Chest Pain

Approximately 13% of COPAXONE 20 mg per mL patients in the 5 placebo-controlled studies compared to 6% of placebo patients, and approximately 2% of patients exposed to COPAXONE 40 mg per mL in a placebo-controlled trial compared to 1% of placebo patients, experienced at least one episode of transient chest pain. While some of these episodes occurred in the context of the Immediate Post-Injection Reaction described above, many did not. The temporal relationship of this chest pain to an injection was not always known. The pain was usually transient, often unassociated with other symptoms, and appeared to have no clinical sequelae. Some patients experienced more than one such episode, and episodes usually began at least 1 month after the initiation of treatment. The pathogenesis of this symptom is unknown.

Lipoatrophy and Skin Necrosis

At injection sites, localized lipoatrophy and, rarely, injection site skin necrosis may occur. Lipoatrophy occurred in approximately 2% of patients exposed to COPAXONE 20 mg per mL in the 5 placebo-controlled trials compared to none on placebo, and 0.5% of patients exposed to COPAXONE 40 mg per mL in a single placebo-controlled trial and none on placebo. Skin necrosis has only been observed in the postmarketing setting. Lipoatrophy may occur at various times after treatment onset (sometimes after several months) and is thought to be permanent. There is no known therapy for lipoatrophy. To assist in possibly minimizing these events, the patient should be advised to follow proper injection technique and to rotate injection sites with each injection.

Potential Effects on Immune Response

Because COPAXONE can modify immune response, it may interfere with immune functions. For example, treatment with COPAXONE may interfere with the recognition of foreign antigens in a way that would undermine the body’s tumor surveillance and its defenses against infection. There is no evidence that COPAXONE does this, but there has not been a systematic evaluation of this risk. Because COPAXONE is an antigenic material, it is possible that its use may lead to the induction of host responses that are untoward, but systematic surveillance for these effects has not been undertaken.
Although COPAXONE® is intended to minimize the autoimmune response to myelin, there is the possibility that continued alteration of cellular immunity due to chronic treatment with COPAXONE may result in untoward effects. Glatiramer acetate-reactive antibodies are formed in most patients receiving glatiramer acetate. Studies in both the rat and monkey have suggested that immune complexes are deposited in the renal glomeruli. Furthermore, in a controlled trial of 125 RMS patients given COPAXONE 20 mg per mL, subcutaneously every day for 2 years, serum IgG levels reached at least 3 times baseline values in 80% of patients by 3 months of initiation of treatment. By 12 months of treatment, however, 30% of patients still had IgG levels at least 3 times baseline values, and 90% had levels above baseline by 12 months. The antibodies are exclusively of the IgG subtype and predominantly of the IgG-1 subtype. No IgE type antibodies could be detected in any of the 94 sera tested; nevertheless, anaphylaxis can be associated with the administration of most any foreign substance, and therefore, this risk cannot be excluded.

6 ADVERSE REACTIONS

The following serious adverse reactions are described elsewhere in the labeling:
- Immediate Post-Injection Reaction [see Warnings and Precautions (5.1)]
- Chest Pain [see Warnings and Precautions (5.2)]
- Lipatrophy and Skin Necrosis [see Warnings and Precautions (5.3)]
- Potential Effects on Immune Response [see Warnings and Precautions (5.4)]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Incidence in Controlled Clinical Trials

COPAXONE 20 mg per mL per day

Among 563 patients treated with COPAXONE in blinded placebo-controlled trials, approximately 5% of the subjects discontinued treatment because of an adverse reaction. The adverse reactions most commonly associated with discontinuation were: injection site reactions, dyspnea, urticaria, vasodilatation, and hypersensitivity. The most common adverse reactions were: injection site reactions, vasodilatation, rash, dyspnea, and chest pain.

Table 1 lists signs and symptoms that occurred in at least 2% of patients treated with COPAXONE 20 mg per mL in the placebo-controlled trials. These signs and symptoms were numerically more common in patients treated with COPAXONE than in patients treated with placebo. Adverse reactions were usually mild in intensity.

### Table 1: Adverse reactions in controlled clinical trials with an incidence ≥2% of patients and more frequent with COPAXONE (20 mg per mL daily) than with placebo

<table>
<thead>
<tr>
<th>Conditions</th>
<th>COPAXONE 20 mg/mL (n=563)</th>
<th>Placebo (n=564)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood And Lymphatic System Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>7%</td>
<td>3%</td>
</tr>
<tr>
<td>Cardiac Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Palpitations</td>
<td>9%</td>
<td>4%</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>5%</td>
<td>2%</td>
</tr>
<tr>
<td>Eye Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eye Disorder</td>
<td>3%</td>
<td>1%</td>
</tr>
<tr>
<td>Diplopia</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>Gastrointestinal Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>15%</td>
<td>11%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>7%</td>
<td>4%</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>2%</td>
<td>1%</td>
</tr>
<tr>
<td>General Disorders And Administration Site Conditions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injection Site Erythema</td>
<td>43%</td>
<td>10%</td>
</tr>
<tr>
<td>Injection Site Pain</td>
<td>40%</td>
<td>20%</td>
</tr>
<tr>
<td>Injection Site Pruritus</td>
<td>27%</td>
<td>4%</td>
</tr>
<tr>
<td>Injection Site Mass</td>
<td>26%</td>
<td>6%</td>
</tr>
<tr>
<td>Asthenia</td>
<td>22%</td>
<td>21%</td>
</tr>
<tr>
<td>Pain</td>
<td>20%</td>
<td>17%</td>
</tr>
<tr>
<td>Injection Site Edema</td>
<td>19%</td>
<td>4%</td>
</tr>
<tr>
<td>Chest Pain</td>
<td>13%</td>
<td>6%</td>
</tr>
<tr>
<td>Injection Site Inflammation</td>
<td>9%</td>
<td>1%</td>
</tr>
<tr>
<td>Edema</td>
<td>8%</td>
<td>2%</td>
</tr>
<tr>
<td>Injection Site Reaction</td>
<td>8%</td>
<td>1%</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>6%</td>
<td>5%</td>
</tr>
<tr>
<td>Injection Site Hypersensitivity</td>
<td>4%</td>
<td>0%</td>
</tr>
<tr>
<td>Local Reaction</td>
<td>3%</td>
<td>1%</td>
</tr>
<tr>
<td>Chills</td>
<td>3%</td>
<td>1%</td>
</tr>
<tr>
<td>Face Edema</td>
<td>3%</td>
<td>1%</td>
</tr>
<tr>
<td>Edema Peripheral</td>
<td>3%</td>
<td>2%</td>
</tr>
</tbody>
</table>

*Injection site atrophy comprises terms relating to localized lipoatrophy at injection site.*
COPAXONE® (glatiramer acetate injection)

Body as a Whole:
- Infrequent: Abcess
- Infrequent: Injection site hematoma, moon face, cellulitis, herinia, injection site abscess, serum sickness, suicide attempt, injection site hypertrophy, injection site melanosis, lipoma, and photosensitivity reaction.

Cardiovascular:
- Frequent: Hypertension.
- Infrequent: Hypotension, midystolic click, systolic murmur, atrial fibrillation, bradycardia, fourth heart sound, postural hypotension, and varicose veins.

Digestive:
- Infrequent: Dry mouth, stomatitis, burning sensation on tongue, cholecystitis, colitis, esophageal ulcer, esophagitis, gastrointestinal carcinoma, gum hemorrhage, hepatomegaly, increased appetite, melena, mouth ulceration, pancreas disorder, pancreatitis, rectal hemorrhage, tenesmus, tongue discoloration, and duodenal ulcer.

Endocrine:
- Infrequent: Goiter, hyperthyroidism, and hypothyroidism.

Gastrointestinal:
- Frequent: Bowel urgency, oral moniliasis, salivary gland enlargement, tooth caries, and ulcerative stomatitis.

Hemic and Lymphatic:
- Infrequent: Leukopenia, anemia, cyanosis, eosinophilia, hematemesis, lymphedema, pancytopenia, and splenomegaly.

Metabolic and Nutritional:
- Infrequent: Weight loss, alcohol intolerance, Cushing’s syndrome, gout, abnormal healing, and xanthoma.

Musculoskeletal:
- Infrequent: Arthritis, muscle atrophy, bone pain, bursitis, kidney pain, muscle disorder, myopathy, osteoarthritis, tendon pain, and tenosynovitis.

Nervous:
- Frequent: Abnormal dreams, emotional lability, and stupor.
- Infrequent: Ataxia, convulsion, circumoral paresthesia, depersonalization, hallucinations, hostility, hypokinesia, coma, concentration disorder, facial paralysis, decreased libido, manic reaction, memory impairment, myoclonus, neuralgia, paranoid reaction, paraplegia, psychotic depression, and transient stupor.

Respiratory:
- Infrequent: Hyperventilation and hay fever.
- Infrequent: Asthma, pneumonia, epistaxis, hyperventilation, and voice alteration.

Skin and Appendages:
- Frecuent: Eczema, herpes zoster, pusular rash, skin atrophy, and warth.
- Infrequent: Dry skin, skin hypertrophy, dermatitis, furunculosis, psoriasis, dry eye, keratitis, papular rash, pigmentation, benign skin neoplasm, skin carcinoma, skin striae, and vesiculobullous rash.

Special Senses:
- Frequent: Visual field defect.
- Infrequent: Dry eyes, otitis externa, ptosis, cataract, corneal ulcer, mydriasis, optic neuritis, photosensitivity, and taste loss.

Urogenital:
- Frecuent: Amenorrhea, hematuria, impotence, menstruation, suspicious papanicolaou smear, urinary frequency, and vaginal hemorrhage.
- Infrequent: Vaginitis, flank pain (kidney), abortion, breast engorgement, breast enlargement, carcinoma in situ, cervix, fibrocystic breast, kidney calcui, nocturia, ovarian cyst, priapism, pyelonephritis, abnormal sexual function, and urethritis.

COPAXONE 40 mg per mL three times per week
Among 943 patients treated with COPAXONE 40 mg per mL three times per week in a blinded, placebo-controlled trial, approximately 3% of the subjects discontinued treatment because of an adverse reaction. The most common adverse reactions were injection site reactions, which were also the most common cause of discontinuation. Table 2 lists signs and symptoms that occurred in at least 2% of patients treated with COPAXONE 40 mg per mL in the blinded, placebo-controlled trial. These signs and symptoms were numerically more common in patients treated with COPAXONE 40 mg per mL than in patients treated with placebo. Adverse reactions were usually mild in intensity.

6.2 Postmarketing Experience
The following adverse reactions have been identified during postapproval use of COPAXONE. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Body as a Whole: sapsis; SLE syndrome; hydrocephalus; enlarged abdomen; allergic reaction; anaphylactoid reaction

Cardiovascular System: thrombosis; peripheral vascular disease; pericardial effusion; myocardial infarct; deep thrombophlebitis; coronary occlusion; congestive heart failure; cardiomyopathy; cardiomegaly; arthralgia; angina pectoris

Digestive System: tongue edema; stomach ulcer; hemorrhage; liver function abnormality; liver damage; hepatitis; urticaria; cirrhosis of the liver; cholelithiasis

Hemic and Lymphatic System: thrombocytopenia; lymphoma-like reaction; acute leukemia

Metabolic and Nutritional Disorders: hypercholesterolemia

Musculoskeletal System: rheumatoid arthritis; generalized spasm

Nervous System: myelitis; meningitis; CNS neoplasm; cerebrovascular accident; brain edema; abnormal dreams; aphasia; convolution; neuralgia

Respiratory System: pulmonary embolus; pleural effusion; carcinoma of lung

Special Senses: glaucoma; blindness

Urogenital System: urogenital neoplasm; urinary abnormality; ovarian carcinoma; nephrosis; kidney failure; breast carcinoma; bladder carcinoma; urinary frequency

7 DRUG INTERACTIONS
Interactions between COPAXONE and other drugs have not been fully evaluated. Results from existing clinical trials do not suggest any significant interactions of COPAXONE with therapies commonly used in MS patients, including the concurrent use of corticosteroids for up to 28 days. COPAXONE has not been formally evaluated in combination with interferon beta.

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
Administration of glatiramer acetate by subcutaneous injection to pregnant rats and rabbits resulted in no adverse effects on offspring development. Therefore, there are no adverse effects on the offspring of females treated with COPAXONE during pregnancy provided continuous therapy is continued. Administration of glatiramer acetate to pregnant rabbits resulted in no adverse effects on offspring development. There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies do not always predict the outcome of human exposure, COPAXONE should be used during pregnancy only if clearly needed.

8.2 Lactation
It is not known whether glatiramer acetate is excreted in human milk. Because many drugs are excreted in human milk, and because of the potential for serious adverse reactions in breast-feeding infants from glatiramer acetate, a decision should be made whether to discontinue breastfeeding or to discontinue the drug, taking into account the importance of the drug to the mother.

8.3 Pediatric Use
Established efficacy of COPAXONE for multiple sclerosis has been demonstrated in patients 18 to 50 years of age. There is no information available on the safety of COPAXONE use in patients below age 18 or above age 50, and no information available on the safety of COPAXONE use in pediatric patients with other conditions.

8.4 Geriatric Use
Ninety-eight percent of patients in this clinical trial were Caucasian and the majority of these were between the ages of 18 and 50. Consequently, data are inadequate to perform an analysis of the adverse reaction incidence related to clinically-relevant age groups.

8.5 Renal Impairment
In rats or rabbits receiving glatiramer acetate by subcutaneous injection during the period of organogenesis, no adverse effects on offspring development were observed at doses up to 37.5 mg/kg/day (18 and 36 times, respectively, the therapeutic human dose of 20 mg/day on a mg/m² basis). In rats receiving subcutaneous glatiramer acetate at doses of 20 mg/kg/day on a mg/m² basis, no new adverse reactions appeared in subjects treated with COPAXONE 40 mg per mL three times per week as compared to subjects treated with COPAXONE 20 mg per mL per day in clinical trials and during postmarketing experience. Data on adverse reactions occurring in the controlled clinical trial of COPAXONE 40 mg per mL were analyzed to evaluate differences based on sex. No clinically significant differences were identified. Ninety-eight percent of patients in this clinical trial were Caucasian and the majority were between the ages of 18 and 50. Consequently, data are inadequate to perform an analysis of the adverse reaction incidence related to clinically-relevant age groups.
COPAXONE® (glatiramer acetate injection)

**11 DESCRIPTION**
Glatiramer acetate, the active ingredient of COPAXONE, consists of the acetate salts of synthetic polypeptides, containing four naturally occurring amino acids: L-glutamic acid, L-lysine, L-tyrosine, and L-lysine with an average molar fraction of 0.141, 0.427, 0.095, and 0.338, respectively. The average molecular weight of glatiramer acetate is 5,000–9,000 daltons. Glatiramer acetate is identified by specific antibodies. Chemical to alter natural acetate is designated L-glutamic acid perimer. There is no evidence that glatiramer acetate is determined by its ability to block the induction of experimental autoimmune encephalomyelitis (EAE) in mice.

**12 CLINICAL PHARMACOLOGY**

**12.1 Mechanism of Action**
The mechanism(s) by which glatiramer acetate exerts its effects in patients with MS are not fully understood. However, glatiramer acetate is thought to act by modifying immune processes that are believed to be responsible for the pathogenesis of MS. This hypothesis is supported by findings of studies that have been carried out to explore the pathogenesis of experimental autoimmune encephalomyelitis, a condition induced in animals through immunization against central nervous system derived material containing myelin and often used as an experimental animal model of MS. Studies in animals and in vitro systems suggest that upon its administration, glatiramer acetate-specific suppressor T-cells are induced and activated in the periphery. Because glatiramer acetate can modify immune functions, concerns exist about its potential to alter naturally occurring immune responses. There is no evidence that glatiramer acetate does this, but this has not been systematically evaluated [see Warnings and Precautions (5.4)].

**12.2 Pharmacokinetics**
Results obtained in pharmacokinetic studies performed in humans (healthy volunteers) and animals support that a substantial fraction of the therapeutic dose delivered to patients subcutaneously is hydrolyzed locally. Larger fragments of glatiramer acetate can be recognized by glatiramer acetate-reactive antibodies. Some fraction of the injected material, either intact or partially hydrolyzed, is presumed to enter the systemic circulation intact.

**13 NONCLINICAL TOXICOLOGY**
In a 2-year carcinogenicity study, mice were administered up to 60 mg/kg/day glatiramer acetate by subcutaneous injection (up to 15 times the human therapeutic dose of 20 mg/day on a mg/m² basis). No increase in systemic neoplasms was observed. In males receiving the 60-mg/kg/day dose, there was an increased incidence of fibrosarcomas at the injection sites. These sarcomas were associated with skin damage precipitated by repetitive injections of an irritant over a limited skin area. In a 2-year carcinogenicity study, rats were administered up to 30 mg/kg/day glatiramer acetate by subcutaneous injection (up to 15 times the human therapeutic dose on a mg/m² basis). No increase in neoplasms was observed. Glatiramer acetate was not mutagenic in in vitro Ames test, mouse lymphoma tk assays. Glatiramer acetate was clastogenic in two separate in vitro chromosomal aberration assays in cultured human lymphocytes but not clastogenic in an in vivo mouse bone marrow micronucleus assay. When glatiramer acetate was administered by subcutaneous injection prior to and during mating (males and females) and throughout gestation and lactation (females) at doses up to 36 mg/kg/day (18 times the human therapeutic dose on a mg/m² basis) no adverse effects were observed on reproductive or developmental parameters.

**14 CLINICAL STUDIES**
Evidence supporting the effectiveness of COPAXONE derives from five placebo-controlled trials, four of which used a COPAXONE dose of 20 mg per mL three times per day and one of which used a COPAXONE dose of 40 mg per mL three times per week.

**14.1 Study 1**
Study 1 was performed at a single center. Fifty patients were enrolled and randomized to receive daily doses of either COPAXONE, 20 mg per mL subcutaneously, or placebo (COPAXONE: n=25; placebo: n=25). Patients were diagnosed with RRMS by standard criteria, and had at least 2 exacerbations during the 2 years immediately preceding enrollment. Patients were ambulatory, as evidenced by a score of no more than 6 on the Kurtzke Disability Scale Score (DSS), a standard scale ranging from 0–Normal to 10–Death due to MS. A score of 6 is defined as one at which a patient is still ambulatory with assistance; a score of 7 means the patient must use a wheelchair. Patients were examined every 3 months for 2 years, as well as within several days of a presumed exacerbation. To confirm an exacerbation, a blinded neurologist had to document objective neurologic signs, as well as document the existence of other criteria (e.g., the persistence of the neurological signs for at least 48 hours). The protocol-specified primary outcome measure was the proportion of patients in each treatment group who remained exacerbation free for the 2 years of the trial, but two other important outcomes were also specified as endpoints: the frequency of attacks during the trial, and the change in the number of attacks compared with the number which occurred during the previous 2 years. Table 3 presents the values of the three outcomes described above, as well as several protocol-specified secondary measures. These values are based on the intent-to-treat population (i.e., all patients who received at least 1 dose of treatment and who had at least 1 on-treatment assessment).

**Table 3: Study 1 Efficacy Results**

<table>
<thead>
<tr>
<th>COPAXONE 20 mg/mL (n=25)</th>
<th>Placebo (n=25)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Relapse-Free Patients</td>
<td>14/25 (56%)</td>
<td>7/25 (28%)</td>
</tr>
<tr>
<td>Mean Relapse Frequency</td>
<td>0.6/2 years</td>
<td>2.4/2 years</td>
</tr>
<tr>
<td>Reduction in Relapse Rate</td>
<td>3.2</td>
<td>1.6</td>
</tr>
<tr>
<td>Median Time to First Relapse (days)</td>
<td>&gt;700</td>
<td>150</td>
</tr>
<tr>
<td>% of Progression-Free* Patients</td>
<td>20/25 (80%)</td>
<td>13/25 (52%)</td>
</tr>
</tbody>
</table>

*Progression was defined as an increase of at least 1 point on the DSS, persisting for at least 3 consecutive months.

Study 2 was a multicenter trial of similar design which was performed in 11 US centers. A total of 251 patients (COPAXONE: n=125; placebo: n=126) were enrolled. Table 4 presents the values of this outcome for the intent-to-treat population, as well as several secondary measures:

**Table 4: Study 2 Efficacy Results**

<table>
<thead>
<tr>
<th>COPAXONE 20 mg/mL (n=125)</th>
<th>Placebo (n=126)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean No. of Relapses</td>
<td>1.19/2 years</td>
<td>1.68/2 years</td>
</tr>
<tr>
<td>% Relapse-Free Patients</td>
<td>42/125 (34%)</td>
<td>34/126 (27%)</td>
</tr>
<tr>
<td>Median Time to First Relapse (days)</td>
<td>287</td>
<td>198</td>
</tr>
<tr>
<td>% of Progression-Free Patients</td>
<td>98/125 (78%)</td>
<td>95/126 (75%)</td>
</tr>
<tr>
<td>Mean Change in DSS</td>
<td>-0.05</td>
<td>+0.21</td>
</tr>
</tbody>
</table>

In both studies, COPAXONE exhibited a clear beneficial effect on relapse rate, and it is based on this evidence that COPAXONE is considered effective.

In Study 3, 481 patients who had recently (within 90 days) experienced an isolated demyelinating event and who had lesions typical of multiple sclerosis on brain MRI were randomized to receive either COPAXONE 20 mg per mL (n=243) or placebo (n=238). The primary outcome measure was time to development of a second exacerbation. Patients were followed for up to three years or until they reached the primary endpoint. Secondary outcomes were brain MRI measures, including number of new lesions and lesion volume. Time to development of a second exacerbation was significantly delayed in patients treated with COPAXONE compared to placebo (Hazard Ratio = 0.55; 95% confidence interval 0.40 to 0.77; Figure 1). The Kaplan-Meier estimates of the percentage of patients developing a relapse within 36 months were 42.9% in the placebo group and 24.7% in the COPAXONE group.
Patients treated with COPAXONE demonstrated fewer new T2 lesions at the last observation (rate ratio 0.41; confidence interval 0.28 to 0.58; p < 0.0001). Additionally, baseline-adjusted T2 lesion volume at the last observation was lower for patients treated with COPAXONE (ratio of 0.89; confidence interval 0.84 to 0.94; p = 0.0001).

Study 4 was a multinational study in which MRI variables were used both as primary and secondary endpoints. A total of 239 patients with RRMS (COPAXONE: n=119; placebo: n=120) were randomized. Inclusion criteria were similar to those in the second study with the additional criterion that patients had to have at least one Gd-enhancing lesion on the screening MRI. The patients were treated in a double-blind manner for nine months, during which they underwent monthly MRI scanning. The primary endpoint for the double-blind phase was the total cumulative number of T1 Gd-enhancing lesions over the nine months. Table 5 summarizes the results for the primary outcome measure monitored during the trial for the intent-to-treat cohort.

<table>
<thead>
<tr>
<th>Table 5: Study 4 MRI Results</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<tr>
<td>Medians of the Cumulative Number of T1 Gd-Enhancing Lesions</td>
</tr>
</tbody>
</table>

Figure 2 displays the results of the primary outcome on a monthly basis.

**Figure 2:** Median Cumulative Number of Gd-Enhancing Lesions

<table>
<thead>
<tr>
<th>Table 6: Study 5 Efficacy and MRI Results</th>
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</thead>
<tbody>
<tr>
<td>COPAXONE 40 mg/mL (n=943)</td>
</tr>
<tr>
<td>Clinical Endpoints</td>
</tr>
<tr>
<td>Adjusted Mean Estimates</td>
</tr>
<tr>
<td>MRI Endpoints</td>
</tr>
<tr>
<td>Adjusted Mean Estimates</td>
</tr>
<tr>
<td>Cumulative number of enhancing lesions on T1-weighted images at Months 6 and 12</td>
</tr>
</tbody>
</table>

16 HOW SUPPLIED/STORAGE AND HANDLING

COPAXONE (glatiramer acetate injection) is a clear, colorless to slightly yellow, sterile, nonpyrogenic solution supplied as:
- 20 mg per mL in a single-dose, prefilled syringe with a white plunger, in individual blister packages supplied in 30-count cartons (NDC 68546-325-12).
- 40 mg per mL in a single-dose, prefilled syringe with a blue plunger, in individual blister packages supplied in 12-count cartons (NDC 68546-325-12).

Store COPAXONE refrigerated at 2°C to 8°C (36°F to 46°F). If needed, the patient may store COPAXONE at room temperature, 15°C to 30°C (59°F to 86°F), for up to one month, but refrigeration is preferred. Avoid exposure to higher temperatures or intense light. Do not freeze COPAXONE. If a COPAXONE syringe freezes, it should be discarded.

17 PATIENT COUNSELING INFORMATION

Advisers of patients should read the FDA-approved patient labeling (Patient Information and Instructions for Use).

Immediate Post-Injection Reaction

Advisers of patients that COPAXONE may cause various symptoms after injection, including flushing, chest pain, palpitations, tachycardia, anxiety, dyspnea, constriction of the throat, and urticaria. These symptoms occur within seconds to minutes after injection and are generally transient and self-limited and do not require specific treatment. Inform patients that these symptoms may occur early or may have their onset several months after the initiation of treatment. A patient may experience one or several episodes of these symptoms.

Chest Pain

Advisers of patients that they may experience transient chest pain either as part of the Immediate Post-Injection Reaction or in isolation. Inform patients that the pain should be transient. Some patients may experience more than one such episode, usually beginning at least one month after the initiation of treatment. Patients should be advised to seek medical attention if they experience chest pain of unusual duration or intensity.

Lipoatrophy and Skin Necrosis at Injection Site

Advisers of patients that localized lipoatrophy, and rarely, skin necrosis may occur at injection sites. Advise patients to follow proper injection technique and to rotate injection areas and sites with each injection to minimize these risks.

Pregnancy

Advisers that if they are pregnant or plan to become pregnant while taking COPAXONE they should inform their physician.

Instruct patients to read the COPAXONE Patient Information leaflet carefully.

COPAXONE 20 mg per mL and COPAXONE 40 mg per mL are not interchangeable.

COPAXONE 20 mg per mL is administered daily and COPAXONE 40 mg per mL is administered three times per week. Caution patients to use aseptic technique. The first injection should be performed under the supervision of a health care professional. Instruct patients against the reuse of needles or syringes. Instruct patients in safe disposal procedures.

Storage Conditions

Advisers that the recommended storage condition for COPAXONE is refrigeration at 36°F to 46°F (2°C to 8°C). If needed, the patient may store COPAXONE at room temperature, 59°F to 86°F (15°C to 30°C), for up to one month, but refrigeration is preferred. COPAXONE should not be exposed to higher temperatures or intense light. Do not freeze COPAXONE.

Marketed by: Teva Neuroscience, Inc., Overland Park, KS 66211
Distributed by: Teva Pharmaceuticals USA, Inc., North Wales, PA 19454
Product of Israel
COP-004
COPAXONE® (glatiramer acetate injection)

Patient Information
COPAXONE (co-PAX-own)
(glutiram acetate injection)
for subcutaneous use

Read this Patient Information before you start using COPAXONE and each time you get a refill. There may be new information. This information does not take the place of talking with your doctor about your medical condition or your treatment.

What is COPAXONE?
COPAXONE is a prescription medicine that is used to treat relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. It is not known if COPAXONE is safe and effective in children under 18 years of age.

Who should not use COPAXONE?
• Do not use COPAXONE if you are allergic to glatiramer acetate, mannitol or any of the ingredients in COPAXONE. See the end of this leaflet for a complete list of the ingredients in COPAXONE.

What should I tell my doctor before using COPAXONE?
Before you use COPAXONE, tell your doctor if you:
• are pregnant or plan to become pregnant. It is not known if COPAXONE will harm your unborn baby.
• are breastfeeding or plan to breastfeed. It is not known if COPAXONE passes into your breast milk. Talk to your doctor about the best way to feed your baby while using COPAXONE.

Tell your doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. COPAXONE may affect the way other medicines work, and other medicines may affect how COPAXONE works.

Know the medicines you take. Keep a list of your medicines with you to show your doctor and pharmacist when you get a new medicine.

How should I use COPAXONE?
• For detailed instructions, see the Instructions for Use at the end of this leaflet for complete information on how to use COPAXONE.
• Your doctor will tell you how much COPAXONE to use and when to use it.
• COPAXONE is given by injection under your skin (subcutaneously).
• Use COPAXONE exactly as your doctor tells you to use it.
• Since every body type is different, talk with your doctor about the injection areas that are best for you.
• You should receive your first dose of COPAXONE with a doctor or nurse present. This might be at your doctor’s office or with a visiting home health nurse who will teach you how to give your COPAXONE injections.

What are the possible side effects of COPAXONE?
COPAXONE may cause serious side effects, including:
• Immediate Post-Injection Reactions. Serious side effects may happen right after or within minutes after you inject COPAXONE at any time during your course of treatment. Call your doctor right away if you have any of these immediate post-injection reaction symptoms including:
  ◦ redness to your cheeks or other parts of the body (flushing)
  ◦ chest pain
  ◦ fast heart beat
  ◦ anxiety
  ◦ breathing problems or tightness in your throat
  ◦ swelling, rash, hives, or itching
If you have symptoms of an immediate post-injection reaction, do not give yourself more injections until a doctor tells you to.
• Chest Pain. You can have chest pain as part of an immediate post-injection reaction or by itself. This type of chest pain usually lasts a few minutes and can begin around 1 month after you start using COPAXONE. Call your doctor right away if you have chest pain while using COPAXONE.

• Damage to your skin. Damage to the fatty tissue just under your skin’s surface (lipodystrophy) and, rarely, death of your skin tissue (necrosis) can happen when you use COPAXONE. Damage to the fatty tissue under your skin can cause a “dent” at the injection site that may not go away. You can reduce your chance of developing these problems by:
  ◦ following your doctor’s instructions for how to use COPAXONE
  ◦ choosing a different injection area each time you use COPAXONE. See Step 4 in the Instructions for Use, “Choose your injection area.”
The most common side effects of COPAXONE include:
• skin problems at your injection site including:
  ◦ redness
  ◦ pain
  ◦ swelling
  ◦ itching
  ◦ lumps
• rash
• shortness of breath
• flushing (vasodilation)

Tell your doctor if you have any side effect that bothers you or that does not go away. These are not all the possible side effects of COPAXONE. For more information, ask your doctor or pharmacist.

How should I store COPAXONE?
• Store COPAXONE in the refrigerator between 36°F to 46°F (2°C to 8°C).
• When you are not able to refrigerate COPAXONE, you may store it for up to 1 month at room temperature between 59°F to 86°F (15°C to 30°C).
• Protect COPAXONE from light or high temperature.
• Do not freeze COPAXONE syringes. If a syringe freezes, throw it away in a sharps disposal container. See Step 13 in the Instructions for Use, “Dispose of your needles and syringes.”

Keep COPAXONE and all medicines out of the reach of children.

General information about the safe and effective use of COPAXONE.
Medicines are sometimes prescribed for purposes other than those listed in a Patient Information Leaflet. Do not use COPAXONE for a condition for which it was not prescribed. Do not give COPAXONE to other people, even if they have the same symptoms as you have. It may harm them.

This Patient Information Leaflet summarizes the most important information about COPAXONE. If you would like more information, talk with your doctor. You can ask your pharmacist or doctor for information about COPAXONE that is written for health professionals. For more information, go to www.copaxone.com or call 1-800-887-8100.

What are the ingredients in COPAXONE?
Active ingredient: glatiramer acetate
Inactive ingredients: mannitol COPPL-004
Revised: July 2019
Instructions for Use

COPAXONE (co-PAX-own) (glatiramer acetate injection) for subcutaneous use

For subcutaneous injection only.
Do not inject COPAXONE in your veins (intravenously).
Do not re-use your COPAXONE prefilled syringes.
Do not share your COPAXONE prefilled syringes with another person. You may give another person an infection or get an infection from them.
You should receive your first dose of COPAXONE with a doctor or nurse present. This might be at your doctor’s office or with a visiting home health nurse who will show you how to give your own injections.
COPAXONE comes in either a 20 mg Prefilled Syringe with needle attached or a 40 mg Prefilled Syringe with needle attached. How often a dose is given depends on the product strength that is prescribed. Your doctor will prescribe the correct dose for you.

Instructions for Using Your COPAXONE 20 mg Prefilled Syringe:
• COPAXONE 20 mg is injected 1 time each day, in the fatty layer under your skin (subcutaneously).
• Each COPAXONE 20 mg prefilled syringe is for single use (1 time use) only.
• The COPAXONE 20 mg dose is packaged in boxes of 30 prefilled syringes with needles attached. COPAXONE 20 mg prefilled syringes have white plungers.

Instructions for Using Your COPAXONE 40 mg Prefilled Syringe:
• COPAXONE 40 mg is injected 3 times each week, in the fatty layer under your skin (subcutaneously).
• COPAXONE 40 mg should be given on the same 3 days each week, if possible for example, Monday, Wednesday, and Friday. Give your COPAXONE injections at least 48 hours (2 days) apart.
• Each COPAXONE 40 mg prefilled syringe is for single use (1 time use) only.
• The COPAXONE 40 mg dose is packaged in boxes of 12 prefilled syringes with needles attached. COPAXONE 40 mg prefilled syringes have blue plungers.

How do I inject COPAXONE?

Step 1: Gather the supplies you will need to inject COPAXONE. See Figure A.
• 1 blister pack with a COPAXONE Prefilled Syringe with needle attached
• Alcohol wipe (not supplied)
• Dry cotton ball (not supplied)
• A place to record your injections, like a notebook (not supplied)
• Sharps disposal container (not supplied). See Step 13 below, "Dispose of your needles and syringes."

Step 2: Remove only 1 blister pack from the COPAXONE prefilled syringe carton. See Figure B.

Step 3: Look closely at your COPAXONE prefilled syringe.
• There may be small air bubbles in the syringe. Do not try to push the air bubble from the syringe before giving your injection so you do not lose any medicine.
• Check the liquid medicine in the syringe before you give your injection. The liquid in the syringe should look clear, and colorless, and may look slightly yellow. If the liquid is cloudy or contains any particles, do not use the syringe and throw it away in a sharps disposal container. See Step 13 below, “Dispose of your needles and syringes.”

Step 4: Choose your injection area. See Figure C.
See the injection areas you should use on your body. Talk with your doctor about the injection areas that are best for you.
• The possible injection areas on your body include (See Figure C):
  ◦ your stomach area (abdomen) around the belly button
  ◦ the back of your upper arms
  ◦ upper hips (below your waist)
  ◦ your thighs (above your knees)

Step 5: Prepare to give your injection.
• There are some injection areas on your body that are hard to reach (like the back of your arm). You may need help from someone who has been instructed on how to give your injection if you cannot reach certain injection areas.
• Do not inject in sites where the skin has scarring or “dents”. Using scarred or dented skin for your injections may make your skin worse.
Step 6: Clean your injection site.
- Clean the injection site using the alcohol wipe and allow your skin to air dry. See Figure D.

Step 7: Pick up the syringe with 1 hand and hold it like a pencil. Remove the needle cover with your other hand and set it aside. See Figure E.

Step 8: Pinch about a 2 inch fold of skin between your thumb and index finger. See Figure F.

Step 9: Giving your injection.
- Rest the heel of your hand holding the syringe against your skin at the injection site. Insert the needle at a 90 degree angle straight into your skin. See Figure G.
- When the needle is all the way into your skin, release the fold of skin. See Figure H.

Step 10: Give your COPAXONE injection.
To inject the medicine, hold the syringe steady and slowly push down the plunger. See Figure I.

Step 11: Remove the needle.
After you have injected all of the medicine, pull the needle straight out. See Figure J.

Step 12: Use a clean, dry cotton ball to gently press on the injection site for a few seconds. Do not rub the injection site or re-use the needle or syringe. See Figure K.

Step 13: Dispose of your needles and syringes.
- Put your used needles and syringes in a FDA-cleared sharps disposal container right away after use. Do not throw away (dispose of) loose needles and syringes in your household trash.
- If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:
  - made of a heavy-duty plastic,
  - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
  - upright and stable during use,
  - leak-resistant, and
  - properly labeled to warn of hazardous waste inside the container.
- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: http://www.fda.gov/safesharpsdisposal.
- Do not dispose of your used sharps disposal container in your household trash unless your community guidelines permit this. Do not recycle your used sharps disposal container.

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

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