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® (glatiramer acetate injection) is prescription medicine used for the treatment of people with relapsing forms of multiple sclerosis (MS).

Important Safety Information

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

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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\textsuperscript{2-4}

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.\textsuperscript{3}
   - Contains melanin, which protects you from harmful ultraviolet (UV) rays.\textsuperscript{3}
   - Contains keratin, a protein cell that gives the skin its toughness.\textsuperscript{5}
   - Protects you from most bacteria, viruses, and other foreign substances.\textsuperscript{3}
   - Protects the internal organs, muscles, nerves, and blood vessels.\textsuperscript{3}

2. **Dermis**: the thick elastic inner layer.\textsuperscript{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\textsuperscript{®} is injected.\textsuperscript{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\textsuperscript{®} (glatiramer acetate injection) is for subcutaneous injection only.

Please see Important Safety Information on Page 11, and 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 skin7

- 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 smoke7

- 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 includes8,9:

- 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.).
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. 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.

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.

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.

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 accompanying full Prescribing Information.
Injection Site Rotation

Rotation matters¹

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 accompanying full Prescribing Information.

Rotating your injection sites¹

1 ABDOMEN  Avoid about 2 inches around the belly button.
2 RIGHT THIGH About 2 inches above knee and 2 inches below groin.
3 LEFT THIGH About 2 inches above knee and 2 inches below groin.
4 LEFT ARM  Fleshy part of the upper back portion of arm.
5 RIGHT ARM Fleshy part of the upper back portion of arm.
6 LEFT HIP  Fleshy area of the upper hip, always below the waist.
7 RIGHT HIP  Fleshy area of the upper hip, always below the waist.

FRONT

BACK
Teva's Shared Solutions® 1-on-1 Injection Training

Whether you have been on therapy for a long time or are just 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 at any time throughout your COPAXONE® experience. 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 at any time during your COPAXONE® treatment experience.

Please see Important Safety Information on Page 11, and 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.

Please see Important Safety Information on Page 11, and accompanying full Prescribing Information.
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.

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

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.

It may be helpful to use warm compresses before injection and cold compresses after injection for up to 5 minutes.

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.

Please see Important Safety Information on Page 11, and accompanying full Prescribing Information.
**Common Injection Site Reactions**

**Inflammation or swelling**
Swelling or tenderness of the skin at the injection site.

**Lumps**
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.

- To prevent inflammation, the area should be sufficiently warmed before injection.
- Apply an ice pack to the area for 5 minutes (not direct contact) after injection.

**Itching at the injection site**
Itching can occur at the injection site following the injection of COPAXONE® (glatiramer acetate injection).

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

- 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.

Other common side effects of COPAXONE® include flushing, rash, shortness of breath, and chest pain. These are not all of the possible side effects of COPAXONE®. For a complete list, ask your doctor or pharmacist. Tell your doctor about any side effects you have while taking COPAXONE®.
Use
COPAXONE® (glatiramer acetate injection) is prescription medicine used for the treatment of people with relapsing forms of multiple sclerosis (MS).

Important Safety Information
Do not take COPAXONE® if you are allergic to glatiramer acetate or mannitol.

Some patients report a short-term reaction right after or within minutes after injecting COPAXONE®. This reaction can involve flushing (feeling of warmth and/or redness), chest tightness or pain, fast heart beat, anxiety, and trouble breathing. These symptoms generally appear within seconds to minutes of an injection, last about 15 minutes, and do not require specific treatment. During the postmarketing period, there have been reports of patients with similar symptoms who received emergency medical care. If symptoms become severe, call the emergency phone number in your area. Call your doctor right away if you develop hives, skin rash with irritation, dizziness, sweating, chest pain, trouble breathing, or severe pain at the injection site. If any of the above occurs, do not give yourself any more injections until your doctor tells you to begin again.

Chest pain may occur either as part of the immediate post-injection reaction or on its own. This pain should only last a few minutes. You may experience more than one such episode, usually beginning at least one month after starting treatment. Tell your doctor if you experience chest pain that lasts for a long time or feels very intense.

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.

The most common side effects of COPAXONE® include redness, pain, swelling, itching, or a lump at the site of injection, flushing, rash, shortness of breath, and chest pain. These are not all of the possible side effects of COPAXONE®. For a complete list, ask your doctor or pharmacist. Tell your doctor about any side effects you have while taking COPAXONE®.

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 see accompanying full Prescribing Information for Teva’s COPAXONE®.

References:

© 2019 Teva Neuroscience, Inc. COP-45817 March 2019 autoject® for glass syringe is a registered trademark of Owen Mumford, Ltd. Available by prescription only. Apple is a registered trademark of Apple Inc. App Store is a service mark of Apple Inc. Google Play and the Google Play logo are trademarks of Google LLC.
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 (e.g., 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
COPAXONE (glatiramer acetate injection) is indicated for the treatment of patients with relapsing forms of multiple sclerosis (1).

**1 INDICATIONS AND USAGE**

COPAXONE (glatiramer acetate injection) is indicated for the treatment of patients with relapsing forms of multiple sclerosis.

**2 DOSAGE AND ADMINISTRATION**

**2.1 Recommended Dose**

COPAXONE is for subcutaneous use only. Do not administer intravenously. The dosing schedule depends on the product strength that is selected. The recommended doses are:

- **COPAXONE 20 mg/mL per day**
- **COPAXONE 40 mg/mL three times per week**

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

**3 CONTRAINDICATIONS**

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

**5 WARNINGS AND PRECAUTIONS**

**5.1 Immediate Post-Injection Reaction**

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, rush, 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, vasodilatation, rush, dyspnea, and chest pain.

**5.2 Chest Pain**

Chest pain, usually transient, has been observed in approximately 13% of COPAXONE 20 mg/mL patients in the 5 placebo-controlled trials compared to 6% of placebo patients, and approximately 2% of patients exposed to COPAXONE 40 mg/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.

**5.3 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/mL in a placebo-controlled trial compared to 0.5% of patients exposed to COPAXONE 40 mg/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.

**5.4 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.

**8 USE IN SPECIFIC POPULATIONS**

**8.1 Pregnancy**

**8.2 Labor and Delivery**

**8.3 Nursing Mothers**

**8.4 Pediatric Use**

**8.5 Geriatric Use**

**8.6 Use in Patients with Impaired Renal Function**

**13 NONCLINICAL TOXICOLOGY**

**14 CLINICAL STUDIES**

**16 HOW SUPPLIED/STORAGE AND HANDLING**

**17 PATIENT COUNSELING INFORMATION**

*Sections or subsections omitted from the full prescribing information are not listed.*

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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 RRMS 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 had IgG levels at least 3 times baseline values, and 90% had levels above baseline in 80% of patients by 3 months.

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)]
- Lipotrophy 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, dyspepsia, urticaria, vasodilatation, and hypersensitivity. The most common adverse reactions were: injection site reactions, vasodilatation, rash, dyspepsia, 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: 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>System Disorders</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>Lymphadenopathy 7% 3%</td>
<td></td>
</tr>
<tr>
<td>Cardiac Disorders</td>
<td>Palpitations 9% 4%</td>
<td></td>
</tr>
<tr>
<td>Tachycardia 5% 2%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eye Disorders</td>
<td>Eye Disorder 3% 1%</td>
<td></td>
</tr>
<tr>
<td>Diplopia 3% 2%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal Disorders</td>
<td>Nausea 15% 11%</td>
<td></td>
</tr>
<tr>
<td>Vomiting 7% 4%</td>
<td></td>
<td></td>
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<tr>
<td>Dysphagia 2% 1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>General Disorders And Administration Site Conditions</td>
<td>Injection Site Erythema 43% 10%</td>
<td></td>
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<tr>
<td>Injection Site Pain 40% 20%</td>
<td></td>
<td></td>
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<tr>
<td>Injection Site Pruritus 27% 4%</td>
<td></td>
<td></td>
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<tr>
<td>Injection Site Mass 26% 6%</td>
<td></td>
<td></td>
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<tr>
<td>Asthenia 22% 21%</td>
<td></td>
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<tr>
<td>Pain 20% 17%</td>
<td></td>
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<tr>
<td>Injection Site Edema 19% 4%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chest Pain 13% 6%</td>
<td></td>
<td></td>
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<tr>
<td>Injection Site Inflammation 9% 1%</td>
<td></td>
<td></td>
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<tr>
<td>Edema 8% 2%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injection Site Reaction 8% 1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pyrexia 6% 5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injection Site Hypersensitivity 4% 0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local Reaction 3% 1%</td>
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<td></td>
</tr>
<tr>
<td>Chills 3% 1%</td>
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<td></td>
</tr>
<tr>
<td>Face Edema 3% 1%</td>
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<tr>
<td>Edema Peripheral 3% 2%</td>
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</tbody>
</table>

*Injection site atrophy comprises terms relating to localized lipoatrophy at injection site

Adverse reactions which occurred only in 4 to 5 more subjects in the COPAXONE group than in the placebo group (less than 1% difference), but for which a relationship to COPAXONE could not be excluded, were arthralgia and herpes simplex.

Other adverse reactions were reported in at least 1/100 patients participating in the clinical program for COPAXONE. Clinically-significant laboratory values for hematologic, chemical, and urinalysis were similar for both COPAXONE and placebo groups in blinded clinical trials. In controlled trials one patient discontinued treatment due to thrombocytopenia (16 x10^9/L), which resolved after discontinuation of treatment.

Data on adverse reactions occurring in the controlled clinical trials of COPAXONE 20 mg per mL were analyzed to evaluate differences based on sex. No clinically-significant differences were identified. Ninety-six percent of patients in these clinical trials were Caucasian. The majority of patients treated with COPAXONE were between the ages of 18 and 45. Consequently, data are inadequate to perform an analysis of the adverse reaction incidence related to clinically-relevant age subgroups.

Other Adverse Reactions

In the paragraphs that follow, the frequencies of less commonly reported adverse clinical reactions are presented. Because the reports include reactions observed in open and uncontrolled premarketing studies (n=979), the role of COPAXONE in their causation cannot be reliably determined. Furthermore, variability associated with adverse reaction reporting, the terminology used to describe adverse reactions, etc., limit the value of the quantitative frequency estimates provided. Reaction frequencies are calculated as the number of patients who used COPAXONE and reported a reaction divided by the total number of patients exposed to COPAXONE. All reported reactions are included except those already listed in the previous table, those too general to be informative, and those not reasonably associated with the use of the drug. Reactions are further classified within body system categories and enumerated in order of decreasing frequency using the following definitions: Frequent adverse reactions are defined as those occurring in at least 1/100 patients and infrequent adverse reactions are those occurring in 1/100 to 1/1000 patients.
COPAXONE® (glatiramer acetate injection)

Body as a Whole:
Frequent: Abcess
Infrequent: Injection site hemotoma, moon face, cellullitis, hernia, 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:
Frequent: 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: 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, osteomyelitis, tendon pain, and tenosynovitis.

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

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

Skin and Appendages:
Frequent: Eczema, herpes zoster, purulent rash, skin atrophy, and warts.
Infrequent: Dry skin, skin hypotrophy, dermatitis, furunculosis, psoriasis, angiodema, contact dermatitis, erythema nodosum, fungal dermatitis, maculopapular 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, photophobia, and taste loss.

Urogenital:
Frequent: Amenorrhea, hematuria, impotence, menstruation, suspicious papanico-loua smear, urinary frequency, and vaginal hemorrhage.
Infrequent: Vaginitis, flank pain (kidney), abortion, breast engorgement, breast enlargement, carcinoma in situ cervix, fibrocystic breast, kidney calculus, 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 in the 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.

Table 2: Adverse reactions in a controlled clinical trial with an incidence ≥2% of patients and more frequent with COPAXONE® (40 mg per mL three times per week) than with placebo

<table>
<thead>
<tr>
<th>Condition</th>
<th>COPAXONE® 40 mg/mL (n=943)</th>
<th>Placebo (n=461)</th>
</tr>
</thead>
<tbody>
<tr>
<td>General Disorders And Administration Site Conditions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injection Site Erythema</td>
<td>22%</td>
<td>2%</td>
</tr>
<tr>
<td>Injection Site Pain</td>
<td>10%</td>
<td>2%</td>
</tr>
<tr>
<td>Injection Site Mass</td>
<td>6%</td>
<td>0%</td>
</tr>
<tr>
<td>Injection Site Pruritus</td>
<td>6%</td>
<td>0%</td>
</tr>
<tr>
<td>Injection Site Edema</td>
<td>6%</td>
<td>0%</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>Influenza-like Illness</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>Injection Site Inflammation</td>
<td>2%</td>
<td>0%</td>
</tr>
<tr>
<td>Chills</td>
<td>2%</td>
<td>0%</td>
</tr>
<tr>
<td>Chest Pain</td>
<td>2%</td>
<td>1%</td>
</tr>
<tr>
<td>Respiratory, Thoracic and Mediastinal Disorders</td>
<td>Dyspnea</td>
<td></td>
</tr>
<tr>
<td>Vasodilatation</td>
<td>3%</td>
<td>0%</td>
</tr>
<tr>
<td>Gastrointestinal Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>2%</td>
<td>1%</td>
</tr>
<tr>
<td>Skin And Subcutaneous Tissue Disorders</td>
<td>Erythema</td>
<td></td>
</tr>
<tr>
<td>Rash</td>
<td>2%</td>
<td>0%</td>
</tr>
</tbody>
</table>

No new adverse reactions were identified 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 age. 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.

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 thrombophilias; coronary occlusion; congestive heart failure; cardiomyopathy; cardiomegaly; arthrythmia; angina pectoris
Digestive System: tongue edema; stomach ulcer; hemorrhage; liver function abnormality; liver damage; hepatitis; urticaria; cirsosis of the liver; cholelithiasis
Hemic and Lymphatic System: thrombocytopenia; lymphoma-like reaction; acute leukemia
Metabolic and Nutritional Disorders: hypercholerosterolemia
Musculoskeletal System: rheumatoid arthritis; generalized spasm
Nervous System: myelitis; meningitis; CNS neoplasm; cerebrovascular accident; brain edema; abnormal dreams; aphasia; convulsion; neuralgia
Respiratory System: pulmonary embolus; pleural effusion; carcinoma of lung
Special Senses: glaucoma; blindness
Urogenital System: urogenital neoplasm; urine 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
Pregnancy Category B.
Administration of glatiramer acetate by subcutaneous injection to pregnant rats and rabbits resulted in no adverse effects on offspring development. There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, COPAXONE® should be used during pregnancy only if clearly needed.

In rats or rabbits receiving glatiramer acetate by subcutaneous injection during the period of organogenesis, no adverse effects on embryo-fetal 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...
COPAXONE® (glatiramer acetate injection)

doses of up to 36 mg/kg from day 15 of pregnancy throughout lactation, no significant effects on delivery or on offspring growth and development were observed.

8.2 Labor and Delivery
The effects of COPAXONE on labor and delivery in pregnant women are unknown.

8.3 Nursing Mothers
It is not known if glatiramer acetate is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when COPAXONE is administered to a nursing woman.

8.4 Pediatric Use
The safety and effectiveness of COPAXONE have not been established in patients under 18 years of age.

8.5 Geriatric Use
COPAXONE has not been studied in elderly patients.

8.6 Use in Patients with Impaired Renal Function
The pharmacokinetics of glatiramer acetate in patients with impaired renal function have not been determined.

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-alanine, L-lysine, and L-tyrosine 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 alteration or degradation of the synthetic polypeptides, containing four naturally occurring amino acids: L-glutamic acid polymer with L-alanine, L-lysine and L-tyrosine, acetate (salt). Its structural formula is:

\[(\text{Glutf, Ala, Lys, Tyr}), \cdot \text{CH}_2\text{COOH}\]

COPAXONE is a clear, colorless to slightly yellow, sterile, nonpyrogenic solution for injection containing glatiramer acetate (C5H9NO4 C3H7NO2 • C6H14N2O2 • C2H4O2 x), L-glutamic acid (C5H9NO4), L-alanine (C3H7NO2), L-lysine (C6H14N2O2), L-tyrosine (C2H4O2 x), and 40 mg of mannitol per mL. The pH of the solutions is approximately 5.5 to 7.0. The biological activity of glatiramer acetate is determined by its ability to block the induction of experimental autoimmune encephalomyelitis (EAÉ) 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 lymphatic circulation, enabling it to reach regional lymph nodes, and some may enter the systemic circulation intact.

13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
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/kg/day, there was an increased incidence of fibrosarcomas at the injection sites. These sarcomas were associated with skin necrosis and ulcers at the injection site. 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/kg 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 subcutaneously and one of which used a COPAXONE dose of 40 mg per mL three times per week.

COPAXONE 20 mg per mL per day

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 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 neurologic 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>
<thead>
<tr>
<th>Study 1 Efficacy Results</th>
<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>
<td>0.085</td>
</tr>
<tr>
<td>Mean Relapse Frequency</td>
<td>0.62/years</td>
<td>2.4/years</td>
<td>0.005</td>
</tr>
<tr>
<td>Reduction in Relapse Rate Compared to Prestudy</td>
<td>3.2</td>
<td>1.6</td>
<td>0.025</td>
</tr>
<tr>
<td>Median Time to First Relapse (days)</td>
<td>&gt;700</td>
<td>150</td>
<td>0.03</td>
</tr>
<tr>
<td>% of Progression-Free* Patients</td>
<td>20/25 (80%)</td>
<td>13/25 (52%)</td>
<td>0.07</td>
</tr>
<tr>
<td>Progression was defined as an increase of at least 1 point on the DSS, persisting for at least 3 consecutive months.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 4 presents the values of this outcome for the intent-to-treat population, as well as several secondary measures.

<table>
<thead>
<tr>
<th>Study 2 Efficacy Results</th>
<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>
<td>0.055</td>
</tr>
<tr>
<td>% Relapse-Free Patients</td>
<td>42/125 (34%)</td>
<td>34/126 (27%)</td>
<td>0.25</td>
</tr>
<tr>
<td>Median Time to First Relapse (days)</td>
<td>287</td>
<td>198</td>
<td>0.23</td>
</tr>
<tr>
<td>% of Progression-Free Patients</td>
<td>98/125 (78%)</td>
<td>95/126 (75%)</td>
<td>0.48</td>
</tr>
<tr>
<td>Mean Change in DSS</td>
<td>-0.05</td>
<td>-0.21</td>
<td>0.023</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 T2 lesions and T2 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 0.59; 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 parameters 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 5: Study 4 MRI Results

<table>
<thead>
<tr>
<th>COPAXONE 20 mg/mL (n=119)</th>
<th>Placebo (n=120)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medians of the Cumulative Number of T1 Gd-Enhancing Lesions</td>
<td>11</td>
<td>17</td>
</tr>
</tbody>
</table>

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

### Immediate Post-Injection Reaction

Advise 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**

Advise 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**

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

**Pregnancy**

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

**Instructions for Use**

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 to rotate injection areas and sites with each injection. Caution patients against the reuse of needles or syringes. Instruct patients in safe disposal procedures.

**Storage Conditions**

Advise patients 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, 70°F to 86°F (21°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.
COPAXONE® (glatiramer acetate injection)

Patient Information
COPAXONE (co-PAX-own)
glatiramer 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 prescription medicine used for the treatment of people with relapsing forms of multiple sclerosis (MS).

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.
- have symptoms of an immediate post-injection reaction. 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.
- have skin problems at your injection site including:
  - redness
  - pain
  - swelling
  - itching
  - lumps
- have symptoms 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.

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
- 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.

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

COPCL-003
Revised: September 2018
COPAXONE® (glatiramer acetate injection)

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.

**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.

Marketed by: Teva Neuroscience, Inc., Overland Park, KS 66211
Distributed by: Teva Pharmaceuticals USA, Inc., North Wales, PA 19454
Product of Israel
COPIFU-001
Revised: August 2016
COP-45616