COPAXONE® (glatiramer acetate injection)

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 and Administration

For subcutaneous injection only; doses are not interchangeable.

COPAXONE 20 mg/mL, three times per week
Before use, allow the solution to warm to room temperature.

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

ADVERSE REACTIONS

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.

Chest pain, usually transient.

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

COPAXONE can modify immune response.

Hepatic Injury: If signs or symptoms of hepatic dysfunction occur, consider discontinuing COPAXONE.

DOSE 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

Revised: 2/2023

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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 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% still had IgG levels above baseline by 12 months. The antibodies are exclusively of the IgG subtype and predominancy of the IgG-1 subtype. No IgG type antibodies could be detected in any of the 94 sera tested; nevertheless, anaphylaxis can be associated with the administration of any foreign substance, and therefore, this risk cannot be excluded.

5.5 Hepatic Injury

Cases of hepatic injury, some severe, including liver failure and hepatitis with jaundice, have been reported with COPAXONE. Hepatic injury has occurred from days to years after initiating treatment with COPAXONE. If signs or symptoms of liver dysfunction occur, consider discontinuation of COPAXONE. Hepatic injury has been reported in patients treated with COPAXONE. If signs or symptoms of liver dysfunction occur, consider discontinuation of COPAXONE. If signs or symptoms of liver dysfunction occur, consider discontinuation of COPAXONE.

6 ADVERSE REACTIONS

The following serious adverse reactions are described elsewhere in the labeling:

- Injection Site Reactions: Hypersensitivity
- Gastrointestinal Disorders: Nausea
- Immune System Disorders: Infection
- Renal And Urinary Disorders: Micturition

COPAXONE. Clinically-significant laboratory values for hematology, chemistry, and urinalysis were excluded, were arthralgia and herpes simplex.

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>Medical Category</th>
<th>COPAXONE 20 mg/mL (n=563) %</th>
<th>Placebo (n=564) %</th>
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<tr>
<td>Blood And Lymphatic System Disorders</td>
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<td>Lymphadenopathy</td>
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<td>Palpitations</td>
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<td>5</td>
<td>2</td>
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<tr>
<td>Eye Disorders</td>
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<td></td>
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<tr>
<td>Diplopia</td>
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<td>2</td>
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<tr>
<td>Gastrointestinal Disorders</td>
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<tr>
<td>Nausea</td>
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<tr>
<td>Vomiting</td>
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<td>1</td>
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<td>General Disorders And Administration Site Conditions</td>
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<td>Injection Site Erythema</td>
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<td>Injection Site Pruritus</td>
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<td>Injection Site Mass</td>
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<td>Injection Site Atropy*</td>
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<td>0</td>
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<tr>
<td>Immune System Disorders</td>
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<td></td>
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<tr>
<td>Hypersensitivity</td>
<td>3</td>
<td>2</td>
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<td>Infections And Infestations</td>
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<td>Vaginal Candidiasatis</td>
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<td>Metabolism And Nutrition Disorders</td>
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<td>Musculoskeletal And Connective Tissue Disorders</td>
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<td>Back Pain</td>
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<td>Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps)</td>
<td>Benign Neoplasm of Skin</td>
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<td>Nervous System Disorders</td>
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<td>Tremor</td>
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<td>2</td>
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<tr>
<td>Migraine</td>
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<td>2</td>
</tr>
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<td>Syncope</td>
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<tr>
<td>Anxiety</td>
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<td>10</td>
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<td>Nervousness</td>
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<tr>
<td>Renal And Urinary Disorders</td>
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<td>Micturition Urgency</td>
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<td>Respiratory, Thoracic And Mediastinal Disorders</td>
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<td>Laryngospasm</td>
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<tr>
<td>Rash</td>
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<td>Skin And Subcutaneous Tissue Disorders</td>
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<td>Pruritus</td>
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<td>Urticaria</td>
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<td>Vascular Disorders</td>
<td></td>
<td></td>
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<tr>
<td>Vasodilatation</td>
<td>20</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.

Laboratory analyses were performed on all patients participating in the clinical program for COPAXONE. Clinically-significant laboratory values for hematology, chemistry, and urinalysis were similar for both COPAXONE and placebo groups in blinded clinical trials. In controlled trials one patient discontinued treatment due to thrombocytopenia (10 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 1/1,000 patients.

Body as a Whole:

Frequent: Abscess
Infrequent: Injection site hematomat, moon face, cellulitis, hermia, 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, cholecytitis, 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.

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
COPAXONE® (glatiramer acetate injection)

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: sepsis; SLE syndrome; hydrocephalus; enlarged abdomen; allergic reaction; anaphylactoid reaction

Cardiovascular System: thrombosis; peripheral vascular disease; pericardial effusion; myocardial infarct; deep thrombembolitis; coronary occlusion; congestive heart failure; cardiomyopathy; cardiologygia; arrhythmia; angina pectoris

Digestive System: tongue edema; stomach ulcer; hemorrhage; eructation

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

Hepatobiliary Disorders: cholelitiasis; liver function abnormality; cirrhosis of the liver; hepatitis; hepatic injury [see Warnings and Precautions (5.5)]

Metabolic and Nutritional Disorders: hypercholesterolemia

Musculoskeletal System: rheumatoid arthritis; generalized spasms

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: ureteral 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

Risk Summary

Available human data on the use of COPAXONE in pregnant women are not sufficient to support conclusions about drug-associated risk for major birth defects and miscarriage. Administration of glatiramer acetate by subcutaneous injection to pregnant rats and rabbits resulted in no adverse effects on embryofetal or offspring development (see Data). The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Human Data

There are no adequate and well-controlled studies of COPAXONE in pregnant women. The available postmarketing reports, case series, and small cohort studies do not provide sufficient information to support conclusions about drug-associated risk for major birth defects and miscarriage.

Animal Data

In rats or rabbits receiving glatiramer acetate by subcutaneous injection during the period of organogenesis, no adverse effects on embryofetal development were observed at doses up to 375 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 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 Lactation

Risk Summary

There are no data on the presence of glatiramer acetate in human milk. Based on the low systemic exposure because of substantial local hydrolysis of glatiramer acetate following subcutaneous administration, breastfeeding is not expected to result in clinically relevant exposure of the infant to the drug (see Clinical Pharmacology (2.3)). There are no data on the effects of glatiramer acetate on milk production.

The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for COPAXONE and any potential adverse effects on the breastfed infant from COPAXONE or from the underlying maternal condition.

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-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 the drug is 2,000 – 5,000 daltons. Glatiramer acetate is identified by specific antibodies. Chemically, glatiramer acetate is designated L-glutamic acid polymer with L-alanine, L-lysine, and L-tyrosine, with L-lysine as the salt. Its structural formula is:

\[
(C_5H_9NO_4)_n\cdot(C_3H_7NO_2)\cdot(C_6H_14N_2O_2)\cdot(C_2H_4O_2)^{n-3}
\]

COPAXONE is a clear, colorless to slightly yellow sterile, nonpyrogenic solution for subcutaneous injection. Each 1 mL of COPAXONE solution contains 20 mg or 40 mg of glatiramer acetate and the following inactive ingredient: 40 mg of mannitol. 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 (EAE) in mice.
COPAXONE® (glatiramer acetate injection)

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 had been carried out to explore the pathogenesis of experimental autoimmune encephalomyelitis, a condition induced in mice 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 suggest 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 circuit.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

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/m^2 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/m^2 basis). No increase in neoplasms was observed.

Mutagenesis

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.

Impairment of Fertility

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/m^2 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, each of which used a COPAXONE dose of 20 mg per mL per day 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 at least 2 exacerbations during the previous 2 years. Patients 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 TI 6-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.

Patients treated with COPAXONE demonstrated fewer new TI lesions at the last observation (rate ratio 0.41; confidence interval 0.28 to 0.59; p < 0.0001). Additionally, baseline-adjusted TI 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).

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

Figure 2: Median Cumulative Number of 6-Gd-Enhancing Lesions

Patients treated with COPAXONE demonstrated fewer new TI lesions at the last observation (rate ratio 0.41; confidence interval 0.28 to 0.59; p < 0.0001). Additionally, baseline-adjusted TI 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).

Figure 1: Time to Second Exacerbation

Figure 1: 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.
COPAXONE® (glatiramer acetate injection)

COPAXONE® 40 mg per mL, three times per week

Study 5 was a double-blind, placebo-controlled, multinational study with a total of 1404 patients with MS who were randomized in a 2:1 ratio to receive either COPAXONE® 40 mg per mL (n=943) or placebo (n=461) three times a week for 12 months. Patients had a median of 2 relapses in the 2 years prior to screening and had not received any interferon-beta for at least 2 months prior to screening. Baseline EDSS scores ranged from 0 to 5.5 with a median of 2.5. Neurological evaluations were performed at baseline, every three months, and at unscheduled visits for suspected relapse or early termination. MRI was performed at baseline, months 6 and 12, or early termination. A total of 91% of those assigned to COPAXONE® and 93% of those assigned to placebo completed treatment at 12 months.

The primary efficacy outcome was the number of confirmed relapses (persistance of neurological symptoms for at least 48 hours confirmed on examination with objective signs). The effect of COPAXONE® on several magnetic resonance imaging (MRI) variables, including number of new or enlarging T2 lesions and number of enhancing lesions on T1-weighted images, was also measured at months 6 and 12.

Table 6: Study 5 Efficacy and MRI Results

<table>
<thead>
<tr>
<th>Clinical Endpoints</th>
<th>COPAXONE® 40 mg/mL (n=943)</th>
<th>Placebo (n=461)</th>
<th>P-Value</th>
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<tr>
<td>Adjusted Mean Estimates</td>
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<td>0.505</td>
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<td>Relative risk reduction</td>
<td>34%</td>
<td>5.692</td>
<td>&lt;0.0001</td>
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<tr>
<th>MRI Endpoints</th>
<th>COPAXONE® 40 mg/mL (n=943)</th>
<th>Placebo (n=461)</th>
<th>P-Value</th>
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<tr>
<td>Cumulative number of new or enlarging T2 lesions at Months 6 and 12</td>
<td>3.650</td>
<td>5.792</td>
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<tr>
<td>Adjusted Mean Estimates</td>
<td>35%</td>
<td>5.692</td>
<td>&lt;0.0001</td>
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<tr>
<td>Relative risk reduction</td>
<td>35%</td>
<td>5.692</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cumulative number of enhancing lesions on T1-weighted images at Months 6 and 12</td>
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<td>1.639</td>
<td>&lt;0.0001</td>
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<tr>
<td>Adjusted Mean Estimates</td>
<td>45%</td>
<td>1.639</td>
<td>&lt;0.0001</td>
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16 HOW SUPPLIED/STORAGE AND HANDLING

COPAXONE® (glatiramer acetate injection) is a clear, colorless to slightly yellow, sterile, nonpyrogenic solution supplied as:
- 20 mg/mL in a single-dose, prefilled syringe with a blue plunger, in individual blister packages supplied in 30-count cartons (NDC 68546-337-30).
- 40 mg/mL in a single-dose, prefilled syringe with a blue plunger, in individual blister packages supplied in 12-count cartons (NDC 68546-325-12).

An optional autoinjector is available by prescription separately (see Dosage and Administration (2.2)). Ensure TEsVax COPAXONE® is used with a compatible autoinjector if an optional autoinjector is prescribed (see Patient Counseling Information (7.7)).

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

Advise the patient to read the FDA-approved patient labeling (Patient Information and Instructions for Use).

Optional Autoinjector

Advise patients with new or existing glatiramer acetate prescriptions to consult their pharmacist or healthcare provider about using an optional prescribed compatible autoinjector device. Advise patients that not all optional prescribed autoinjectors are compatible with all glatiramer acetate products and using an autoinjector that is not compatible may increase the risk for medication errors, such as missing a dose or administration of a partial dose.

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 may 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.

Lipatrophy and Skin Necrosis at Injection Site

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

Hepatic Injury

Advise patients that hepatic injury, including hepatic failure and hepatitis with jaundice, has been reported with the use of COPAXONE®. Educate patients about the signs and symptoms of hepatic injury and instruct patients to report them immediately to their healthcare provider (see Warning and Precautions (5.5)).

Pregnancy

Advise patients that if they are pregnant or plan to become pregnant while taking COPAXONE® they should inform their physician (see Use in Specific Populations (8.1)).

Lactation

Advise patients to notify their healthcare provider if they are breastfeeding or intend to breastfeed during COPAXONE® therapy (see Use in Specific Populations (8.2)).

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 healthcare 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, 55°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®.

17 PATIENT COUNSELING INFORMATION

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 complete list of the ingredients in COPAXONE® (see Use in Specific Populations (8.4)).

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, but any amount is expected to be low if it does. 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.

Manufactured for: Teva Neuroscience, Inc., Parsippany, NJ 07054
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COP-011

Patient Information

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

Table 6: Study 5 Efficacy and MRI Results

<table>
<thead>
<tr>
<th>Clinical Endpoints</th>
<th>COPAXONE® 40 mg/mL (n=943)</th>
<th>Placebo (n=461)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjusted Mean Estimates</td>
<td>0.331</td>
<td>0.505</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Relative risk reduction</td>
<td>34%</td>
<td>5.692</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MRI Endpoints</th>
<th>COPAXONE® 40 mg/mL (n=943)</th>
<th>Placebo (n=461)</th>
<th>P-Value</th>
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</thead>
<tbody>
<tr>
<td>Cumulative number of new or enlarging T2 lesions at Months 6 and 12</td>
<td>3.650</td>
<td>5.792</td>
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<tr>
<td>Adjusted Mean Estimates</td>
<td>35%</td>
<td>5.692</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Relative risk reduction</td>
<td>35%</td>
<td>5.692</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cumulative number of enhancing lesions on T1-weighted images at Months 6 and 12</td>
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<td>1.639</td>
<td>&lt;0.0001</td>
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<tr>
<td>Adjusted Mean Estimates</td>
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<td>1.639</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

5
COPAXONE® (glatiramer acetate injection)

- COPAXONE® can be given using a prefilled syringe or an optional autoinjector that your healthcare provider may prescribe separately for use with COPAXONE.

If you use an autoinjector to give COPAXONE:
- Check with your healthcare provider when you fill or refill your prescription. Make sure the autoinjector you have is the right one for your COPAXONE. Not all optional autoinjectors can be used with all glatiramer acetate products. If you use the wrong autoinjector, you might not get enough medicine from your dose.
- Read your autoinjector instructions for Use and talk to your healthcare provider about the best way for you to use COPAXONE.

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 (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
  - choosing a different injection area each time you use COPAXONE.

See Step 4 in the Instructions for Use, “Choose your injection area”.

- **Liver problems.** Liver problems, including liver failure, can occur with COPAXONE. Call your healthcare provider right away if you have symptoms, such as:
  - nausea
  - loss of appetite
  - tiredness
  - dark colored urine and pale stools
  - yellowing of your skin or the white part of your eye
  - bleeding more easily than normal
  - confusion
  - sleepiness

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.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

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-007
Revised: April 2022

Instructions for Use
COPAXONE® (glatiramer acetate injection)
(co-PAXine)
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.

If you plan to use COPAXONE with an autoinjector that was prescribed separately by your healthcare provider for use with COPAXONE, ask your doctor or pharmacist for Patient Instructions for Use for your device.

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.