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

COPAXONE (glatiramer acetate) solution for subcutaneous injection
Initial U.S. Approval: 1996

----------RECENT MAJOR CHANGES----------
Indications and Usage (1) 2/2009

----------INDICATIONS AND USAGE----------
COPAXONE is indicated for reduction of the frequency of relapses in patients with Relapsing-Remitting Multiple Sclerosis, including patients who have experienced a first clinical episode and have MRI features consistent with multiple sclerosis.

----------DOSAGE AND ADMINISTRATION----------
- For subcutaneous injection only (2.1)
- Recommended dose: 20 mg/day (2.1)
- Before use, allow the solution to warm to room temperature (2.2)

----------DOSAGE FORMS AND STRENGTHS----------
- Prefilled syringe containing 1 mL solution with 20 mg of glatiramer acetate (3)

----------CONTRAINDICATIONS----------
Known hypersensitivity to glatiramer acetate or mannitol (4)

----------WARNINGS AND PRECAUTIONS----------
- Immediate Post-Injection Reaction (flushing, chest pain, palpitations, anxiety, dyspnea, throat constriction, and/or urticaria), generally transient and self-limiting (5.1)
- Chest pain, usually transient (5.2)
- Lipoatrophy and skin necrosis may occur. Instruct patient in proper injection technique and to rotate injection sites daily (5.3)
- COPAXONE can modify immune response (5.4)

----------ADVERSE REACTIONS----------
- In controlled studies, most common adverse reactions (≥10% and ≥1.5 times higher than placebo) were: injection site reactions, vasodilatation, rash, dyspnea, and chest pain (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact TEVA at 1-800-221-4026 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch.*

----------USE IN SPECIFIC POPULATIONS----------
- Nursing Mothers: It is not known if COPAXONE is excreted in human milk (8.3)
- Pediatric Use: The safety and effectiveness of COPAXONE have not been established in patients under 18 years of age (8.4)

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

Revised: [2/2009]

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION
COPAXONE (glatiramer acetate)

1 INDICATIONS AND USAGE

COPAXONE is indicated for reduction of the frequency of relapses in patients with Relapsing-Remitting Multiple Sclerosis (RRMS), including patients who have experienced a first clinical episode and have MRI features consistent with multiple sclerosis.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dose

COPAXONE is for subcutaneous use only. Do not administer intravenously. The recommended dose of COPAXONE is 20 mg/day.

2.2 Instructions for Use

Remove one blister that contains the syringe from the COPAXONE prefilled syringes package. Since this product should be refrigerated, let the prefilled syringe stand at room temperature for 20 minutes to allow the solution to warm to room temperature. Inspect the COPAXONE syringe visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The solution in the syringe should appear clear, colorless to slightly yellow. If particulate matter or discoloration is observed, discard the COPAXONE syringe.

Areas for self-injection include arms, abdomen, hips, and thighs. The prefilled syringe is for single use only. Discard unused portions.

3 DOSAGE FORMS AND STRENGTHS

Single-use prefilled syringe containing 1 mL solution with 20 mg of glatiramer acetate and 40 mg of mannitol.

4 CONTRAINDICATIONS

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

5 WARNINGS AND PRECAUTIONS

5.1 Immediate Post-Injection Reaction

Approximately 16% of patients exposed to COPAXONE in the 5 placebo-controlled trials compared to 4% of those on placebo experienced a constellation of symptoms immediately after injection that included at least two of the following: flushing, chest pain, palpitations, anxiety, dyspnea, constriction of the throat, and urticaria. The symptoms were generally transient and self-limited and did not require treatment. In general, these symptoms have their onset several months after the initiation of treatment, although they may occur earlier, and a given patient may experience one or several episodes of these symptoms. Whether or not any of these symptoms actually represent a specific syndrome is uncertain. During the

postmarketing period, there have been reports of patients with similar symptoms who received emergency medical care.

Whether an immunologic or nonimmunologic mechanism mediates these episodes, or whether several similar episodes seen in a given patient have identical mechanisms, is unknown.

5.2 Chest Pain

Approximately 13% of COPAXONE patients in the 5 placebo-controlled studies compared to 6% of placebo patients experienced at least one episode of what was described as 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 of COPAXONE was not always known. The pain was transient (usually lasting only a few minutes), 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 have been reported during the postmarketing experience. 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 daily.

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.

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 exposed to daily treatment with the recommended dose. 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, 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 lgG subtype and predominantly of the lgG-1 subtype. No lgE type antibodies could be detected in any of the 94 sera tested; nevertheless, anaphylaxis can be associated with the administration of most any foreign substance, and therefore, this risk cannot be excluded.

6 ADVERSE REACTIONS

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 clinical practice.

Incidence in Controlled Clinical Trials

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

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

Table 1: Adverse reactions in controlled clinical trials with an incidence ≥2% of patients and more frequent with COPAXONE than with placebo

		GA 20 mg (N=563)	Placebo (N=564)
Blood And Lymphatic System Disorders	Lymphadenopathy	7%	3%
Cardiac Disorders	Palpitations	9%	4%
	Tachycardia	5%	2%
Eye Disorders	Eye Disorder	3%	1%
	Diplopia	3%	2%
Gastrointestinal Disorders	Nausea	15%	11%
	Vomiting	7%	4%
	Dysphagia	2%	1%

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