Summary

On May 24, 2014, the main drug patent on Teva’s Copaxone® (glatiramer acetate injection) 20mg/mL will expire, allowing generics to become available. In 1996, the US Food and Drug Administration (FDA) approved Teva’s New Drug Application (NDA) for Copaxone, which is not a biologic drug. It is likely that A-rated generics to Copaxone will be approved on, or shortly after May 24, 2014. However, Teva has submitted several Citizen’s Petitions to FDA in attempt to delay approval of generics. This Issues Document is intended to describe the impact of moving from Copaxone to generics and to highlight how Express Scripts’ program offering can help plan sponsors.

Take-Away Points

- Copaxone is a disease-modifying drug administered by subcutaneous (SC) injection to treat relapsing forms of multiple sclerosis (MS).
- Copaxone has been available since 1996 as a 20mg/mL formulation that is administered SC once daily (QD).
- On January 29, 2014, Copaxone 40mg/mL was approved. This high-dose formulation is administered SC three times per week (TIW).
- The patent for Copaxone 20mg/mL expires on May 24, 2014. It is possible that interchangeable generics to Copaxone 20mg/mL SC QD will be approved by FDA at that time. Copaxone 40mg/mL SC TIW will have protection from direct generic competition until at least May 2017, but likely longer following the issuance of additional patents.
- Express Scripts and Accredo have the tools and expertise to help manage MS in light of impending availability of generics formulations of Copaxone.

Copaxone Overview

On December 20, 1996, FDA approved Teva’s NDA for Copaxone 20mg/mL to treat patients with relapsing-remitting MS. Copaxone 20mg/mL is administered QD by SC injection. On January 29, 2014, FDA approved Teva’s supplemental NDA (sNDA) for Copaxone 40mg/mL SC for TIW dosing. Although Copaxone 20mg QD and Copaxone 40mg TIW have not been directly compared in a clinical trial, the safety profile for both formulations is similar. Copaxone 20mg QD and 40mg TIW have similar efficacy (e.g., annualized relapse rates), which is also comparable to efficacy rates reported with interferon beta products. Currently, both Copaxone formulations are available in single-dose, prefilled syringes containing the same active and inactive ingredients (glatiramer acetate and mannitol). Copaxone 20mg/mL was first approved as a lyophilized powder that required reconstitution by the patient prior to self-injection.

Copaxone is a non-biologic disease-modifying medication. Examples of other disease-modifying medications for MS are in Table 1.

Table 1

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Generic Name</th>
<th>Manufacturer</th>
<th>Route*</th>
<th>Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avonex®</td>
<td>interferon beta-1a</td>
<td>Biogen Idec</td>
<td>IM</td>
<td>Once weekly</td>
</tr>
<tr>
<td>Betaseron® / Extavia®</td>
<td>interferon beta-1b</td>
<td>Bayer / Novartis</td>
<td>SC</td>
<td>Every other day</td>
</tr>
<tr>
<td>Copaxone®</td>
<td>glatiramer acetate</td>
<td>Teva</td>
<td>SC</td>
<td>Once daily (20mg) or three times weekly (40mg)</td>
</tr>
<tr>
<td>Rebif®</td>
<td>interferon beta-1a</td>
<td>EMD Serono / Pfizer</td>
<td>SC</td>
<td>Three times weekly</td>
</tr>
<tr>
<td>Tysabri®</td>
<td>natalizumab</td>
<td>Biogen Idec</td>
<td>IV</td>
<td>Once monthly</td>
</tr>
<tr>
<td>Gilenya®</td>
<td>fingolimod</td>
<td>Novartis</td>
<td>Oral</td>
<td>Once daily</td>
</tr>
<tr>
<td>Aubagio®</td>
<td>teriflunomide</td>
<td>Genzyme / Sanofi</td>
<td>Oral</td>
<td>Once daily</td>
</tr>
<tr>
<td>Tecfidera®</td>
<td>dimethyl fumarate</td>
<td>Biogen Idec</td>
<td>Oral</td>
<td>Twice daily</td>
</tr>
</tbody>
</table>

*IM = Intramuscular; IV = Intravenous
Copaxone Generic Outlook

The remaining patents on Copaxone 20mg/mL will expire May 24, 2014. Currently, four manufacturers have publically announced plans to market generics to Copaxone: Momenta/Sandoz, Mylan, Synthon and Dr. Reddy’s. Momenta/Sandoz and Mylan are considered the lead companies developing the generics and continue to anticipate approval of A-rated, substitutable generics to Copaxone 20mg/mL upon the expiration of Copaxone’s patent. The availability of generic Copaxone from the other manufacturers remains somewhat unclear.

In a recent earnings call, Momenta reaffirmed its expectations for launching generics to Copaxone in 2014. The company indicated that its abbreviated NDA (ANDA) is in an FDA prioritized group of applications where there is not yet generic competition. FDA is aware of the Orange Book patent expiration dates for these priority applications and is coordinating its review with those dates in mind. To date, Momenta has not received any questions from FDA that would indicated its generic application is off track. Therefore, the company continues to expect approval of an A-rated generic to Copaxone 20mg/mL this year.

Generic availability, including the number of manufacturers marketing the generics to Copaxone 20mg/mL, is contingent upon final regulatory approval. To date, Teva has filed six Citizen’s Petitions in an attempt to delay FDA’s approval of generics to Copaxone. Momenta expects that FDA will reaffirm its authority to determine “sameness” in approving a generic to Copaxone. However, Teva is expected to exhaust all pathways, both legal and regulatory, in an attempt to delay generics.

Express Scripts’ Response

While supply of generic Copaxone to meet market demand is not yet clear, Express Scripts and Accredo Specialty Pharmacy have the tools and expertise to help manage MS short and long term regardless of these unknowns. Some of the available tools can be found below.

Drug Choices

Express Scripts offers a number of robust utilization management strategies such as Prior Authorization, Preferred Specialty Management and Drug Quantity Management to better manage the evolving MS therapy class. These programs not only ensure clinically appropriate use of MS medications, but will also promote long term use of preferred generic/brand medications.

Additional programs such as copayment differentials, Drug Conversion Programs that target Home Delivery Multi-Source Brands with a DAW1 or DAW2 and Off-Patent Notifications encourage utilization of less expensive generics to Copaxone. These programs include provider outreach, proactive patient engagement, and specialist clinicians who educate and assist patients through the conversion.

Specialty Care Management Programs

Accredo Therapeutic Resource Centers (TRCs) offer specialized clinical care to ensure patients get the specific drug and disease information they need to improve adherence and achieve the best possible outcome from their therapy. Through the Multiple Sclerosis CareLogic program, specialized pharmacists and nurses work with patients who have MS every day. They evaluate newly prescribed medications in concert with patient specific characteristics, such as concomitant medications and comorbid diseases, to ensure an optimal regimen reaches the patient. The Multiple Sclerosis CareLogic program also provides the patient with education about appropriate administration, potential side effects, and management of those side effects as well as the importance of medication adherence.