Development of the First FDA-Approved MS Generic Disease-modifying Therapy: Glatopa® (glatiramer acetate injection)

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In the United States (US), disease-modifying therapy (DMT) costs for multiple sclerosis (MS) continue to rise despite the availability of numerous treatment options, with final-generation DMTs costing approximately $20,000 annually per patient. Copaxone® (glatiramer acetate injection; Teva Pharmaceutical Industries Ltd.) 20 mg/mL has been approved in the US for nearly two decades; the price (ARIP) has more than doubled in the past 5 years. Glatiramer acetate (GA) is a mixture of synthetic polypeptides, made through a chemical synthesis from four amino acids (alanine, glutamic acid, lysine, and tyrosine) without using cellular biologic starting materials (and therefore is not a biologic.) In April 2015, the Food and Drug Administration (FDA) approved the first generic disease-modifying therapy for MS: Glatopa® (GA injection; Sandoz, Inc.) 20 mg/mL. Glatopa is fully substituted for Copaxone® 20 mg/mL for relapsing forms of MS. The exact mechanism of GA is unknown, but GA is believed to exert its biological effects as an antigen-based immunomodulatory agent by targeting multiple pathways on both the innate and adaptive arms of the immune system. This poster reviews the development of Glatopa 20 mg/mL.

BACKGROUND

Glatiramer acetate is a complex mixture of polypeptides (not a biologic) and, consequently, its characterization presented unique challenges not generally unconsidered in generic drug development. Utilizing the Abbreviated New Drug Application (ANDA) regulatory pathway—the pathway used for development and FDA approval of generic drugs in the US—equivalence of Glatopa in Copaxone® 20 mg/mL was shown by starting materials and basic chemistry, structural signatures associated with the process used to manufacture GA, structural properties, and biological and immunological properties. Multiple samples of Glatopa and Copaxone 20 mg/mL were used for analyses. Examples of the structural and functional similarities are shown below; methods for these have been previously published.

METHODS

RESULTS

Glatopa has been available and manufactured in the US for over a year. The content of the Glatopa package insert (PI) is the same as the Copaxone 20 mg PI, and the adverse events received from launch until June 30, 2016 for Glatopa are consistent with what is described in the Copaxone PI.

The estimated savings from January 1, 2016 to present for Glatopa versus the 20 mg dose of Copaxone (~$17,000 annually per patient based on US wholesale acquisition costs).

A comprehensive patient support program has been established for Glatopa, similar to that offered to users of Copaxone.

CONCLUSIONS

The results presented in this poster represent a small portion of the comprehensive set of structural and functional/biological assays that were conducted. Structural properties and biological properties were equivalent across more than 45 tests and biological properties were equivalent across more than 15 assays, including gene expression studies and a well-established animal model of MS.

The development of Glatopa was further confirmed by FDA’s publication of a draft (Product-Specific Approach) document following Glatopa’s approval which provides recommendations for the development of generic biologics based on the demonstration of active pharmaceutical ingredient (API) similarity.

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