Comparative Gene Expression Profiling between a Generic (Glatopa™) and Brand Copaxone® (glatiramer acetate injection)

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**BACKGROUND**

Copaxone® (glatiramer acetate injection, Teva Pharmaceutical Industries Ltd.) has been approved in the U.S. for the treatment of relapsing forms of multiple sclerosis (MS) for nearly two decades. Produced entirely through chemical processes with standard starting materials, it is a mixture of synthetic polyesters of variable molecular weights and sequences and is manufactured from the amino acids L-arginine, L-glutamic acid, L-lysine, and L-tyrosine in a specific molar ratio (1:2).

Copaxone has had price increases of nearly 170% in the past 6 years [3]. Interest in development of more affordable generic versions of glatiramer acetate Copaxone has had price increases of nearly 170% in the past 6 years [3]. Interest in development of more affordable generic versions of glatiramer acetate GA (glatiramer acetate injection; Sandoz, Inc.) is the first generic GA approved by the FDA, and equivalence to Copaxone was established using a comprehensive set of physicochemical (structural) and biological (functional) assays. The objective of the current analysis was to evaluate equivalence of gene expression profiles between Glatopa and Copaxone using microarray technology, which allows for the simultaneous detection of genome-wide perturbations in a biological test system.

**METHODS**

Microarray analysis was performed on murine QA-responsive Th2-polarized T cells, a test system highly relevant to the biology of GA (Figure 3). An Agilent 4x44K single-color hybridization array was designed for murine transcripts containing 39,429 unique probes covering the entire genome was used.

**RESULTS**

- **Gene expression profiles of Glatopa and Copaxone were found to be equivalent in terms of single genes as well as the pathways of glatiramer acetate activation.**

- **Pathway analysis conducted to evaluate changes to genes in T cells and antigen presenting cells (APCs) following repeat exposure to GA.**

- **Statistical evaluation of affected marker genes showed equivalent responses between Glatopa and Copaxone.**

**CONCLUSIONS**

- **Gene expression profiles of Glatopa and Copaxone were found to be equivalent in a well-controlled, scientifically robust study.**

- **These results are supportive of and consistent with results from a larger biobehavioral program that evaluated the equivalence of Glatopa and Copaxone, which consists of multiple complementary molecular, cell-based, and in vivo assays across relevant biologic activities of GA.**

**REFERENCES**


2. Towfic et al. 2014


5. *A* statistical evaluation of affected marker genes showed equivalent responses between Glatopa and Copaxone.

**DISCUSSION**

- **Multiple robust statistical methods demonstrated that the expression of numerous genes was significantly different between Glatopa and Copaxone when compared against media-only control; gene expression profiles induced by Copaxone and the negative control were different, indicating the sensitivity of the test system and the method of analysis; gene expression profiles induced by Glatopa and Copaxone were not significantly different.**

- **Pathway analysis demonstrated generated by Th2 T-helper cell activity and antigen cell presentation were induced by GA. No statistically significant differences were observed between Glatopa and Copaxone in the expression levels (magnitude and direction) of these GA-regulated genes.**

- **These results are supportive of and consistent with results from a larger biobehavioral program that evaluated the equivalence of Glatopa and Copaxone, which consists of multiple complementary molecular, cell-based, and in vivo assays across relevant biologic activities of GA.**

- **Using similar techniques, a recent study [4] showed differences between Copaxone and a non-FDA-approved, another generic GA that is manufactured by Natco Pharma, Ltd. (Hyderabad, India). The study used similar techniques, however the validity of the results are questionable due to flaws in choice of comparator and methodology. Numerous differences between that study and the current study described in Table 1.**

**Table 1: Comparison with Other Glatiramer Acetate Gene Expression Study**

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<th>Comparator</th>
<th>Methodology</th>
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