More Clarity for Complex Biosimilars: Europe Approved the First Follow-On Monoclonal Antibodies – Canada Follows Suit

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Authors: Noel Courage and Ainslie Parsons

Last year, the European Medicines Agency (EMA) granted marketing authorizations to two biosimilar versions of Johnson & Johnson's rheumatoid arthritis blockbuster drug Remicade[1]. The active substance of Remicade is infliximab, a chimeric humane-mouse monoclonal antibody (mAb). Remicade has been authorized in the European Union since August 1999. The EMA's acknowledgment that Celltrion's Remsima and Hospira's Inflectra can be compared to Remicade is the first time that mAbs were deemed to be biosimilar in the EU. In the bigger picture, this provides further insight on the EMA's criteria for approving biosimilars of complex biologics. Canada has now approved the drugs for marketing authorization based on biosimilarity, following the EMEA's lead.

Unlike generic versions of small molecule pharmaceuticals, follow-on versions of biologic drugs (biosimilars) have a similar, but not identical, active ingredient as an approved innovator drug. In particular, there can be differences in structure, formulation, impurities or immunogenicity between the two products which can make it difficult to compare the biosimilar to the innovator drug. The biosimilar manufacturer must provide substantial supporting data to regulators in comparison to conventional follow-on small molecule pharmaceuticals.

The EMA has authorized at least 12 biosimilar medicines to date including biosimilar versions of somatropin (recombinant human growth hormone), filgrastim (granulocyte colony-stimulating factor analog) and epoetin alfa (synthetic erythropoietin). However, mAbs present additional comparability challenges compared to these early commercial biologics given their size and complexity. For example, mAbs can be 10 to 15 times larger than human growth hormone and erythropoietin.

In May of 2012, the EMA released guidance setting out an approval pathway for mAbs (*Guideline on similar biological medicinal products containing monoclonal antibodies – non-clinical and clinical issues*)[2]. The EMA issued its opinions on Remsima and Inflectra by reference to this Guideline. This Guideline, like all the EMA biosimilars guidelines, emphasizes the demonstration of comparability to the reference drug. The EMA found that both Remsima and Inflectra had a comparable quality, safety and efficacy profile to Remicade.

The recommendation by the EMA to approve Remsima and Inflectra provides additional guidance to those planning to market their own biosimilar antibodies. Indeed, it has been estimated that there were at least 49 biosimilar mAbs under development as of September, 2011[3]. It will also be interesting to see how other jurisdictions such as the United States, which introduced a specialized, abbreviated approval pathway for biosimilars in March of 2010[4] but has yet to approve a mAb biosimilar, will treat follow-on antibodies.

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1 http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2013/06/news_detail_001837.jsp&mid=WC0b01ac058004d5c1

2 http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2012/06/WC500128686.pdf

3 Citeline's Pipeline Database, see http://www.pharma-share.com/biosimilar-monoclonal-antibodies-pipeline-major-players-strategies