Regulators Throw Open the Doors to Complex Biosimilars to Reduce Drug Costs

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The US **FDA has now approved** a biosimilar version of infliximab, which is a chimeric human-mouse monoclonal antibody. Celltrion's Inflectra (infliximab-dyyb) can now be marketed in the US by Hospira. Janssen Biotech, Inc. owns the blockbuster initial version of the drug, which it has sold under the brand name Remicade since it was approved in 1998. The Inflectra product was approved for specific indications relating to **conditions** such as Crohn's disease, ulcerative colitis, rheumatoid arthritis and psoriasis.

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 FDA stated that its approval of Inflectra was based on structural and functional characterization, animal study data, human pharmacokinetic and pharmacodynamics data, clinical immunogenicity data and other clinical safety and effectiveness data. No indication was given of the extent of any clinical trial data.

In 2013, the European Medicines Agency (**EMA**) granted marketing authorizations to two biosimilar Celltrion/Hospira versions of infliximab (brand names Remsima and Inflectra). The EMA found that both Remsima and Inflectra had a comparable quality, safety and efficacy profile to Remicade. In 2014, Canada also approved the drugs for marketing authorization based on biosimilarity, following the EMEA's lead.

This is the second biosimilar authorized by the FDA. The EMA has authorized more than a dozen biosimilar medicines to date including biosimilar versions of somatropin (recombinant human growth hormone), filgrastim (granulocyte colony-stimulating factor analog) and epoetin alfa (synthetic erythropoietin).

In the bigger picture, this FDA approval should provide further insight on the FDA's criteria for approving biosimilars of complex biologics. The monoclonal antibody approval is significant from a regulatory perspective because antibodies present additional comparability challenges compared to early commercial biologics which have lesser size and complexity. For example, monoclonal antibodies can be 10 to 15 times larger than the early biosimilars like human growth hormone and erythropoietin. There is a widespread interest in industry for additional guidance to those planning to market their own biosimilar antibodies. It has been estimated that there were at least **49 biosimilar mAbs under development** as of September, 2011.