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Case Update

The U.S. Biosimilars Market is Heating Up: Guidance from the Federal Circuit is Expected Late Spring

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It has been five years to the month since the Biologics Price Competition and Innovation Act ("BPCIA") was signed into law, and March 2015 was the busiest month to date for the emerging U.S. biosimilars market. Currently worth approximately $1 billion a year worldwide, reports predict that this market will be worth at least $20 billion a year by 2020. This provides a strong incentive for companies like Sandoz, Celltrion, Hospira, Eli Lilly, Teva, Apotex, Accord, Ratiopharm, and others who currently market the 19 biosimilar drugs that are on sale in Europe, to seek approval in the lucrative U.S. market.

The FDA Has Approved the First U.S. Biosimilar

As we reported here, the door to the U.S. biosimilars market officially opened on March 6, 2015 with the FDA approval of Sandoz's Zarxio®. Zarxio® (filgrastim) is an analog of a naturally occurring granulocyte-colony stimulating factor ("G-CSF"), a protein that among other things stimulates bone marrow to produce a particular type of white blood cell, and stem cells, and release them into the bloodstream. Zarxio® (marketed in Europe as Zarzio®) is one of eight filgrastim biosimilars that are currently on the market in Europe.

The biologic reference drug for Zarxio® is Amgen's Neupogen®, and Zarxio® has now been approved for all five of the indications on the Neupogen® label, including the treatment of patients with cancer receiving various types of chemotherapy, the treatment of patients with cancer undergoing bone marrow transplantation, and the treatment of patients with various types of neutropenia (a disorder that is characterized by an abnormally low number of a particular type of white blood cells that serve as a primary defense against infection).

Zarxio® Launch is Delayed by Patent Litigation

Zarxio® is now expected to enter the market at the earliest in May 2015, a decision taken by Sandoz in light of pending patent litigation filed by Amgen in October 2014. In that litigation, Amgen alleges, among other things, that Sandoz failed to respect the provisions of the BPCIA because it failed to provide Amgen with a copy of its Biologic License Application ("BLA") and its manufacturing information, and failed to participate in the exchange of patent lists and detailed (in-)validity, (un-) enforce-ability and (non-)infringement contentions set out in Act (informally known as the "patent dance"). Amgen maintains that these failures constitute violations of the BPCIA entitling it, among other things, to a preliminary injunction.

On March 19, Judge Richard Seeborg of the Northern District of California denied that relief, holding that Sandoz was within its rights not to provide its BLA and

manufacturing information to Amgen, and could choose not to participate in the "patent dance." Rejecting Amgen's argument that the relevant provisions of the BPCIA were mandatory, Judge Seeborg found that the procedures set out in the Act were only "'required' where the parties elect to take advantage of their benefits":

"… compliance allows an applicant to enjoy a temporary safe harbor from litigation and, potentially, to resolve or narrow patent disputes outside court proceedings … [if] an applicant does not comply at all with the disclosure procedures, or fails to follow through after having begun the process … the reference product sponsor [can] commence patent litigation immediately … removing (or precluding) availability to the applicant of a litigation safe harbor."

Amgen Inc. et al v. Sandoz Inc. et al, 3:14-cv-04741 (N.D. Cal., March 25, 2015) at 9-10.

Noting that the disclosure and negotiation process set out in the BPCIA "could take up to 230 days," Judge Seeborg observed that a biosimilar applicant "who values expedience over risk mitigation," may (as Sandoz did) "opt to invite suit … soon after filing its BLA with the FDA." *Id.* at 11. The disadvantage with this approach is that such applicants forgo the chance to "preview which patents the reference product sponsor believes are valid and infringed," and forgo "some control over which patents are litigated and when." *Id.*

Judge Seeborg's decision has now been appealed on an expedited schedule to the Federal Circuit. Briefing will be completed by the end of April, and oral argument is expected to promptly follow.

The FDA Weighs in and Defers to the Courts

Shortly after filing its complaint in October 2014, Amgen also filed a Citizen Petition with the FDA, requesting that the FDA require biosimilar applicants to include in their BLA a certification that they will send the reference product sponsor a copy of the BLA and their manufacturing information "within 20 days" after being informed that their application has been accepted for review. On March 25, 2015, the FDA denied this request, stating that the BPCIA "procedures are parallel to, but separate from, the FDA review process," and also noting the ongoing litigation. Docket No. FDA-2014-P-1771, at 4, 3.

Janssen Files Suit Following Celltrion and Hospira's BLA for Infliximib

The Amgen litigation is not the only biosimilar patent infringement litigation that is currently pending in the U.S. On March 6, 2015, Janssen filed suit in the District of Massachusetts against Celltrion and Hospira, relating to their proposed biosimilar of Janssen's biologic, Remicade® (infliximab). *Janssen Biotech, Inc. et al v. Celltrion Healthcare Co., Ltd.* et al, 1:15-cv-10698 (D. Ma.). Similar to Amgen's complaint, Janssen alleges, among other things, that the defendants' refusal to provide a copy of their BLA and manufacturing information, and their refusal to partake in the "patent dance," violates the BPCIA, entitling Janssen to relief, including a preliminary injunction.

Celltrion and Hospira's biosimilar, Remisina®, was approved in Europe in September 2013, and their BLA and Investigational New Drug ("IND") application was accepted by the FDA in October and November 2014.

Infliximab is a chimeric (human/mouse) monoclonal antibody that is approved in the U.S. to treat Crohn's disease, ulcerative colitis, plaque psoriasis, ankylosing spondylitis (a chronic skeletal inflammatory disease), and various forms of arthritis. The FDA Arthritis Advisory Committee was scheduled to discuss the Remisina® BLA

on March 17, 2015. However, this meeting was postponed in light of pending information requests sent by the FDA to the applicants. If approved, Remisina® could be the first biosimilar monoclonal antibody to enter the U.S. market

With a Federal Circuit decision on Zarxio® expected as soon as June, the U.S. biosimilars market is definitely heating up. With 19 biosimilars already on the market in Europe, and a number of relevant U.S. patents set to expire in the next few years, the availability of biosimilars in the U.S. is expected to increase rapidly, and could profoundly change the U.S. biologics market.

About Fitzpatrick:

Fitzpatrick, Cella, Harper & Scinto (www.fitzpatrickcella.com), is a leading national intellectual property law firm with offices in New York, Costa Mesa, California and Washington, D.C. Over half of our approximately 150 attorneys have undergraduate and/or postgraduate degrees in biotechnology, biochemistry, molecular biology, biomedical science, biomedical engineering, molecular pharmacology, genetics, biology, chemistry and related disciplines.

We have extensive experience securing and litigating patent rights concerning all aspects of biopharmaceuticals and biotechnology, including recombinant therapeutic proteins, monoclonal antibodies, DNA sequencing and genomics, and antisense technology.

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