Makers of Humira and Enbrel Using New Drug Patents to Delay Generic Versions

By ANDREW POLLACKJULY 15, 2016

The best-selling drugs Humira and Enbrel have a lot in common. They both use biotechnology to treat rheumatoid arthritis, psoriasis and other autoimmune diseases. And they come with giant price tags approaching $50,000 a year.

Now the two companies behind the competing drugs have found common ground in keeping those prices so high: They are deploying new patents to prevent patients and insurers from getting two essentially generic versions of the drugs for less money.

This week, advisers to the Food and Drug Administration recommended approval of the near generic versions. But the patents could delay introduction. And even if the drugs get to market, some patient groups say they will resist efforts by insurers to force them to use the less expensive drugs.

The various developments show that six years after the Affordable Care Act cleared the way for biosimilars, as the generic versions of biotechnology drugs are called, progress has been slow. Only one biosimilar, a mimic of the white blood cell booster Neupogen, is available to patients.

“It’s a lost opportunity to reduce health care costs,” said Fiona M. Scott Morton, a professor at the Yale School of Management.

By contrast, according to a study she did, biosimilars have been available in Europe for years and have reduced costs for some drugs as much as 80 percent, though in many cases far less.

Humira and Enbrel are biologics, which are complex proteins made in living cells. Seven of the world’s top 10 selling drugs in 2015 were biologics. Humira was No. 1 with $14 billion in global sales and Enbrel was No. 3 at $8.7 billion, according to the website PharmaCompass.

Until the 2010 Affordable Care Act authorized the F.D.A. to approve biosimilars, biologics were insulated from the generic competition. Since then, it has taken time for the F.D.A. to lay out the ground rules for biosimilars. Some rules are still not in place.

Photo

AbbVie’s signature drug Humira was No. 1 in global sales last year with $14 billion.
Credit
David J. Phillip/Associated Press

“They are still behind when it comes to creating the infrastructure to push these molecules ahead,” said Bertrand C. Liang, chairman of a biosimilars council set up by the Generic Pharmaceutical Association.

Things now seem to be heating up, however. A biosimilar that mimics Johnson & Johnson’s autoimmune disease drug Remicade was approved by the F.D.A. in April. It is not yet on the market, in part because of patent issues. But Pfizer, which owns the marketing rights, hints that it is planning to introduce it this year.

There are about 60 biosimilars in clinical trials aimed at approval in the United States or Europe, according to Sanford C. Bernstein & Company, including 13 versions of Humira.

The makers of the brand-name biotechnology drugs for years argued that biologics were such complex molecules that they could not be exactly copied. It is for that reason the copycats are called biosimilars rather than generics.

Still, that argument is now falling by the wayside, in part because some of those same brand-name companies are developing biosimilars themselves.

Amgen, for example, was on both sides of this week’s debates among the F.D.A. advisers. The company developed the Humira biosimilar, but it also owns Enbrel, which is threatened by biosimilars.

At the meeting on Tuesday, the advisory committee voted 26 to 0 that Amgen’s Humira knockoff was similar enough to the original drug to be approved for essentially all uses of Humira. It made that decision even though Amgen had tested the drug in patients with only two of those diseases, rheumatoid arthritis and psoriasis.

The next day it voted 20 to 0 in favor of a broad approval of the Enbrel biosimilar, which was developed by Sandoz, the generic division of Novartis, and tested only in patients with psoriasis.

While the F.D.A. itself is expected to approve the two biosimilars in the coming months, patents might keep them off the market.

If its new patents hold, by 2029, Enbrel will have been on the market without generic competition for 31 years.

Credit

JB Reed/Bloomberg

The main patent on the composition of Humira expires at the end of this year. But AbbVie, the company behind Humira, has amassed more than 70 newer patents, mostly in the last three years, covering formulations of the drug, manufacturing methods and use for specific diseases. It says these ancillary patents should protect its crown jewel, which accounted for 61 percent of its revenue last year, until at least 2022.

“Any company seeking to market a biosimilar version of Humira will have to contend with this extensive patent estate, which AbbVie intends to enforce vigorously,” Richard A. Gonzalez, the company’s chief executive, said last October.

Enbrel's main patent has already expired. But the drug is now protected by two "submarine patents," so called because they wended their way through the patent office over a long period of time, hidden from view. Even though the inventions involved were made in the early 1990s, the patents were not granted until 2011 and 2012 and last until 2028 and 2029.

If those patents hold, by 2029, Enbrel will have been on the market without generic competition for 31 years, far longer than the 12 years of exclusivity for biologics called for in the Affordable Care Act. Humira has been on the market for 14 years.

Humira and Enbrel are direct competitors, but that by itself has not led to much price competition. List prices of the two drugs have been rising in lock step and are nearly triple what they were in early 2008, according to SSR, an investment research firm.

Biosimilar developers might be able to circumvent the ancillary patents and some are challenging their validity at the patent office.

"Biosimilar developers are realizing that these follow-on patents are vulnerable," said Oona Johnstone, a patent lawyer at Wolf Greenfield. However, Amgen failed in its first attempt to invalidate two patents on Humira formulations.

Even if biosimilars get to market, their impact will depend on how widely they are used. At the F.D.A. advisory committee meeting, one issue that could limit the adoption of the biosimilars came into view. Numerous patient and doctor groups argued that insurers should not be allowed to switch patients to a biosimilar if they were doing well on the brand-name drug, because the products are not absolutely identical.

"It may be essentially equivalent to a scientist or an insurance company, but it's not to the patient," said Seth Ginsberg, president of the Global Healthy Living Foundation, a patient advocacy group. The foundation counts AbbVie and Amgen among its corporate sponsors.

https://www.nytimes.com/2016/07/16/business/makers-of-humira-and-enbrel-using-new-drug-patents-to-delay-generic-versions.html?_r=0