

An Introduction to Biosimilars

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What are Biosimilars ?

Roughly equivalent of generics for biologics

Large molecules as opposed to small molecule chemical drugs

Produced in living organisms

Difficulty if not impossible to be identical to originator biologics

Originator biologics vary from batch to batch

Background

- Until the passage of the Patient Protection and Affordable Care Act of 2010 (PPACA), which was included within it the Biologic Price Competition and Innovation Act of 2009 (BPCIA), there was no simple pathway for biosimilars
- To be approved by the FDA biosimilars have to be highly similar to the originator biologic
- Biosimilars have the same properties as the reference drug but because they are produced in living organisms like viruses they are not identical
- Manufacturing is a more significant issue in the case of biologics than for chemical drugs

Background

- Biosimilars are relatively new
- The first approval in the EU was 2006
- The first approval in the U.S. was 2015
- Competition is growing in the EU and for some biosimilars prices have decreased by as much as 80%
- The U.S. started later and its healthcare system is more complex so the market is developing slowly

Background

- The biosimilar market, especially in the U.S., is in its infancy with only 20 biosimilars approved, the first in 2015
- Seven biosimilars are on the market in U.S.
- There is the possibility for even greater innovations as originator firms want to develop new drugs to replace the biologics that are now subject to competition
- Issue: How to balance the dual objectives of competition and innovation
- There are considerable differences and some similarities between the generic and biosimilar markets

Biologics among the Highest Priced Drugs

- Biologics are among the highest priced drugs
- The annual price for Soliris in 2015 was \$536,529 and Naglazyme was \$485,747
- These are the two most expensive biologics
- The tenth most expensive, Revlimid, had an annual price of \$128,666
- However, these are list prices and most are discounted
- Some of these expensive biologics are so-called orphan drugs and are used for a small patient population
- So need high price to get return on investment

Growth of Biologics and Specialty Drugs

- Nearly all of the net increase in drug spending in the U.S. over the last few years has been driven by biologics -- large, complex molecules that are exceedingly expensive to bring to market and manufacturer, but with significant life-saving benefits
- They are large molecule drugs as opposed to small molecule chemical drugs which formerly were the typical drugs.
- These biologics treat some of the most serious illnesses
- Most biologics are specialty drugs
- Specialty medications now account for 44.7 percent of total drug spending, up 3.9 percent from 2017
- Specialty drugs are expected to account for half of total U.S. drug spend by 2020 even though only 1% to 2% of Americans use specialty drugs

Barriers to Biosimilar Entry

- There are many barriers that make biosimilars entry more difficult than generics
- Some are
 - High cost of R&D
 - FDA approval
 - Litigation Issues
 - Originator's Response

Biosimilar Development

- Biosimilars are much more costly to develop and the process takes much longer than generics
- Biosimilar development is expected to cost between \$100 million and \$200 million and take between eight to ten years
- Their complexity makes expertise in manufacturing quite important
- Celltrion has invested \$112 million in the development of Remsima, a biosimilar for Remicade
- Companies experienced in biologic manufacturing will have a learning curve advantage which translates into a cost advantage
- Most entrants into biosimilars are likely to be large, biologic originators for other reference products

FDA Approval

- Must show that biosimilar is highly similar to reference product
- Entry into the biosimilar market also requires establishing manufacturing facilities that must meet FDA requirements regarding “good manufacturing practices”
- Recently there have been manufacturing issues which has kept various biosimilars from getting FDA and EU approval
- Clinical trials are currently needed for approval
- These trials can be quite expensive and often they have difficulty getting enough patients
- With so many biosimilar applications and complexity, FDA resources are becoming strained, leading to delays in the process

Originators' Response

- The originators have actively responded in a variety of ways including
 - Litigation
 - Lowering price and other conduct
 - Developing second generation biologics (biobetters)
 - Patent extension
 - Better devices
 - Reducing the frequency of dosages

Exclusivity Period and Patents

- Economic rationale for exclusivity and patents allow innovator the ability to get a return on investment
- In U.S. newly approved biologics get 12 year market exclusivity from FDA approval and this is not subject to litigation
- Patent rights for 20 years from time of patent application
- Biologics must get FDA approval before marketing drug so effective patent life may be around 10 to 12 years
- Unfortunately, in U.S. often not clear when patents are valid, infringed or patents no longer in effect which can lead to much uncertainty and patent litigation

Litigation

- First biosimilar approved in U.S. in March 2015 delayed until Sept. 2015 because of legal issues
- The Supreme Court decided that biosimilars did not need to wait until approval to give 180 day notification of entry and patent dance is not mandatory
- Pfizer filed an antitrust suit concerning volume discounts, exclusivity and other contract issues
- Between 2011-14 over 90% of initial generic entrants faced patent disputes
- Biosimilars seem to be following same pattern
- Under out of court settlements several companies have agreed not to have their Humira biosimilar enter until 2023.

Pricing Strategies

- Initially in the U.S. the first biosimilar for each reference product has entered at around a 15% discount of the list
- In the case of Remicade biosimilar, Samsung the 2nd biosimilar entered at a 35% discount and Pfizer has matched it
- Coherus is launching its Neulasta biosimilar at 33% discount
- However, unlike the generic market the reference product has also decreased price
- Generally, the reference product firm has already achieved a return on its invest during the time of protection
- It is making a profit since it only needs to cover its marginal costs
- Biosimilar firms have greater investment than generic firms

Market Opportunities

- IMS projects that the global biologic market will exceed \$390 billion by 2020
- By 2025 more than 70% of new drug approvals would be biological products
- U.S. sales in 2014 were around \$200 billion and grew over 10%
- The U.S. is around 50% of biologics market
- Many biologics have sales of over a billion dollars with some over \$10 billion
- Over 30 biologics have lost or will soon lose patent protection which represents \$80 billion
- The reference products for the 5 biosimilars that Sandoz has in its 2020 development portfolio generated nearly \$44 billion in 2015 global sales
- Given the potential market opportunity, there is expected to be an influx of biosimilars into the market

Consumer Welfare Gain

- It is important to note that the primary public policy objective is to increase consumer welfare
- The market share of biosimilars is not a fully informative metric
- The relevant welfare benchmark is not price of the biosimilar relative to the reference product, but the comparison price before competition
- The increase in quantity due to lower prices increases access

Potential Gains from Competition

- Even if the price due to biosimilar competition decreases less than generics
- The savings to consumers and society could be much greater in the case of biosimilars because of their higher prices
- A 20% decrease in \$100,000 biologics is \$20,000 whereas an 80% decrease in \$1k drug is \$800
- The savings to consumers and society could be much greater in the case of biosimilars than for generics because of their higher prices

Potential Gains from Competition

- Biosimilar competition is also expected to result in substantial benefits
- Generic drugs have saved over a trillion dollars in healthcare costs between 2002 and 2011
- According to IMS biosimilars “are expected to deliver total savings of as much as \$110 billion to health systems across Europe and the U.S. through 2020”
- Another benefit from biosimilar competition is an increased interest in developing new drugs by originators as existing drugs lose market share and profits

Future of Pharma is at Stake

- Tradeoff between competition with lower prices and innovation
- Public policy needs to balance these goals
- Despite various barriers to entry
- Competition will lead to lower prices and increase access if the biosimilar experiment succeeds
- Biosimilars are the grand experiment
- Biosimilars are part of the PPACA which currently is being challenged as unconstitutional
- If biosimilar competition does not work may be in for price controls
- This could decrease the incentive to innovate and lead to fewer new drugs being developed