Biosimilar Entry in the US To Date: Good for Competition, Bad for the New Competitors

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Summary

While 2017 has been bad for new biosimilar competitors, it has been good for competition as prices for incumbent drugs such as Remicade has dropped significantly for the first time. Rather than argue for more legal and legislative protection for biosimilars, we argue for a rethinking of competitive strategy on the part of the entrants.

One of the most profound quotes in antitrust law can be found in a 1962 Supreme Court opinion by Chief Justice Earl Warren regarding *Brown Shoe Co. v. United States,* 370 U. S. 320. He argued that the U.S. Congress enacted antitrust laws "for the protection of competition, not competitors."

This idea will being tested to the maximum in the coming years as new biosimilar entrants will have a tough time gaining insurance coverage because of exclusive dealing formulary contracts between incumbents and pharmacy benefit managers (PBMs) and insurance companies.

If manufacturers of biosimilars choose to litigate, we believe that the courts will dismiss antitrust lawsuits summarily based on the now widely accepted Chicago School theories that vertical restraints such exclusive dealing formulary contracts are **presumptively** pro-competitive. (See our recent paper Biosimilars and Exclusive Dealing Antitrust Law: The Case of Pfizer, Inc v Johnson & Johnson et. al.

Price Competition Between Biosimilars and Incumbents

The potential of biosimilars to compete on price has been greatly enhanced by Federal legislation passed as part of the Affordable Care Act of 2010. This legislation greatly abbreviated the FDA approval process for biosimilars by allowing entrants to use test results supplied to the FDA by incumbents.

The accelerated approval process has reduced biosimilar R&D costs by more than 90% from an estimated $2.6 Billion for a new drug to an estimated $100 - $200 Million to develop a biosimilar,

Prior to 2017, most of the attention has focused on the competitive potential of biosimilars. Not much attention had been paid to the potential of incumbents to respond with aggressive price cutting of their own. Also, until this year, not much attention had been paid to the potential of insurance companies and pharmacy benefit managers (PBMs) to drive price competition through exclusive dealing formulary contracts.

This is surprising because there there has been considerable evidence that PBMs have been driving price competition among small molecule brand drugs via exclusive dealing formulary rebate contracts since 2012.

Biosimilars Inflectra® and Renflexis® vs the Incumbent Remicade®

Johnson & Johnson's (J&J) incumbent biologic drug Remicade was approved by the FDA for use in August 1998. It was the first autoimmune drug to be approved in three different therapeutic classes and is used to treat patients with autoimmune diseases

including rheumatoid arthritis, psoriatic arthritis, Crohn's disease, plaque psoriasis, and ulcerative colitis.

In 2016, Remicade was the 5th highest selling drug in the United States with estimated sales of $5.3 Billion. Remicade was J&J's top selling drug, representing 20% of its total global drug sales.

In November 2016, Pfizer introduced Inflectra as the first biosimilar to Remicade. It was followed by the introduction of a second biosimilar called Renflexis in June 2017 by Merck and Samsung Bioepis.

At the time of its introduction, Pfizer list priced Inflectra only 15% below the incumbent, but increased the discount to 35% seven months later to match the list price of the second biosimilar entrant Renflexis.

On September 20, 2017, Pfizer filed a lawsuit Pfizer Inc. v Johnson & Johnson et al (link to the full court filing) claiming that Johnson & Johnson (J&J) violated Section 2 of the Sherman Antitrust Act by monopolizing the market for its incumbent biologic drug Remicade. This was achieved via rebate contracts with the largest insurance companies in the USA that had the effect of excluding from coverage Pfizer's biosimilar drug Inflectra.

Pfizer argued that its rebate offers would have make Inflectra the lower cost drug on a "**unit-for-unit**" basis. But, in our paper dealing with this lawsuit, we presented a spreadsheet (see below) comparing Pfizer's unit rebate offer with an estimate of J&J lump-sum rebate offer estimated at 28% off Remicade's list price contingent on

exclusive coverage.

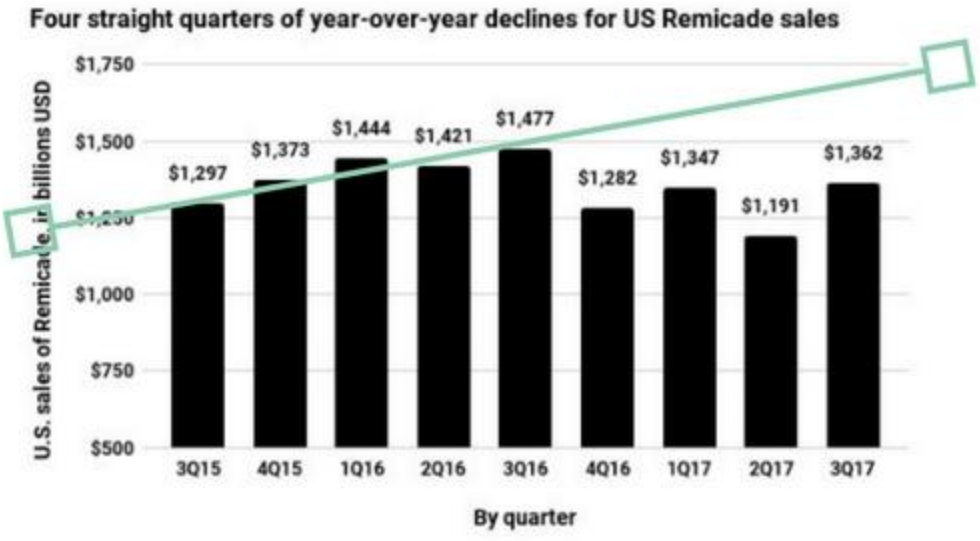
Who is The Low Cost Supplier?				
Manufacturer	J&J	Pfizer		
Drug Name	Remicade	Inflectra		
	Original Biologic	Biosimilar	%	Notes
WAC List Price	$ 1,173	$ 997	15%	% reduction from Remicade
Exclusivity Rebate	$ 2,000,000,000	$ -		
Unit Volume Rebate	$ -	$ 400	40%	Pfizer's Rebate as a % Off List
Vials Sold -- Year	6,000,000	275,000	4%	Inflectra's % of Market - Units
Effective Unit Rebate	$ 333	$ 400		
Effective Unit Net Price	$ 840	$ 597		
"Unit to Unit Comparison"		$ (243)		
Dollars Off List Price	0	$ (48,386,250)		
Dollars In Additional Rebates	$ (2,000,000,000)	$ (110,000,000)		
Total Dollars Off List	$ (2,000,000,000)	$ (158,386,250)		
"Dollars to Dollars Comparison"	$ (1,841,613,750)			
What if? -- Pfizer Rebate at Remicade Volume		$ 2,400,000,000		

We concluded that Remicade was still the low cost choice **on a total dollar basis** and that exclusive dealing contracts between J&J and insurance companies were pro-competitive and not in violation of antitrust laws.

In September 2017, J&J's CFO Dominic Caruso told Wall Street analysts that Remicade sales had dropped only 5% year-over-year. He attributed J&J's success to doing a "pretty good job of contracting for Remicade well in advance of the biosimilar entry from Pfizer." He also attributed J&J's success to natural barriers to biosimilar adoption in general.

With the 5% figure doesn't seem like much, it is masking a larger YoY drop in the net price of Remicade due to the biosimilar entry. Below is a chart of quarterly US sales for Remicade for a full two years from 3Q15 through 3Q17. Note the drop in sales dollars beginning in 4Q16 when the biosimilar was first introduced. A simple projection of sales

from 2015 before the biosimilar entry results results in a “what-if?” no entry estimated 3Q17 US sales for Remicade of around $1,700 Million. While YoY sales from 3Q16 to 3Q17 only dropped 5%, we believe that a more accurate estimate of the effect of biosimilar entry is a 20% decline in sales dollars = (1,700 - 1,362) / 1,362. Again this 20% decline in Remicade sales dollars has to be broken down into quantity changes vs unit price changes.



The competition between Remicade and Inflectra represents the first “clean” case study of biosimilar price competition in the United States. We see several takeaways that future biosimilar entrants might want to keep in mind:

- The Incumbent will already have in place insurance coverage contracts with $100+M lump sum rebates contingent upon exclusivity.
- Entrants should consider adopting a “land and expand” strategy going after coverage for new patients first and being prepared offer rebates that reduce list price an additional 50+%.

The Follow-On Biologic Basaglar® vs the Incumbent Lantus®

Sanofi's Lantus was the first long-acting insulin drug approved by the FDA in April 2000. Since then, there has been a number of other long-acting insulin drugs approved that are in the same therapeutic class: Sanofi's Toujeo (glargine) and Novo Nordisk's Levemir (detemir) and Tresiba (degludec). Because these drugs are self-injectable, they are usually covered by a drug benefit plan managed by PBMs as opposed to a medical benefit plan managed by insurance companies.

While Lantus faces competition from therapeutic equivalents, it has remained the dominant drug in the long-acting insulin class. In 2016, Lantus was the #9 best selling drug in the US with estimated sales around $6 Billion dollars.

On December 15, 2015, Eli Lilly introduced a rapid-acting insulin drug called Basaglar. It is formally classified as a follow-on biologic, not a biosimilar, because it was approved under a different approval process. Notwithstanding the label, this case has relevance to biosimilar competition.

According to Business Insider, Lilly list priced Basaglar only 15% below Lantus at the time of its introduction. The table below summarizes the 2016 list prices of all rapid acting insulin drugs relative to the incumbent and top seller Lantus.

List Price Competition in Rapid Acting Insulin Therapeutic Class - 2016

Pharma Co.	Relation To Incumbent	Drug	WAC List Price as % of Incumbent	
Sanofi	Incumbent	Lantus®	0%	SoloSTAR 1 Box WAC - $272.75
Novo Nordisk	Therapeutic Equiv	Levemir®	6%	
Novo Nordisk	Therapeutic Equiv	Tresiba®	13%	
Sanofi	Therapeutic Equiv	Toujeo®	0%	
Eli Lilly	**Follow-on Biologic**	**Basaglar®**	**-15%**	
	Source: Lantus WAC			
	Source: List Price Comparisons			

According to BioFarmDive, Lantus sales have fallen nearly 17% YoY from 2Q15 to 2Q16. Some of that has been attributed to matching price competition from therapeutic equivalents. Some has been due to quantity reductions as patient have moved to new drugs including Sanofi own drug Toujeo.

It appears that Lilly's tepid list pricing of its biosimilar Basaglar has added nothing to the the price competition (via rebates for formulary placement) that already existed in the rapid-acting insulin therapeutic class.

The fact that incumbent here was facing significant competition before the entry of a biosimilar is probably unique to the insulin class due to a relative lack of patents protecting biologic production processes for insulin.

As a result, the Basaglar entry is not a "clean" case study of biosimilar competition. But, what it demonstrates is that once again list pricing a biosimilar not more than 15% below the list price of the incumbent and playing the rebate game is insufficient to gain much insurance coverage.

This lack of impact is reflected in the recently announced 2018 national formularies of the four largest PBMs. Only CVS Health has decided to include Basaglar and exclude Lantus.

2018 National Formulary for Long-Lasting Insulin Therapeutic Class

Pharma Co.	Relation To Incumben	FDA Approved	Drug	CVS Health		Express Scripts		Prime Therapeutics		OptumRx	
				Included	Excluded	Included	Excluded	Included	Excluded	Included	Excluded
Sanofi	Incumbent	4-2000	Lantus®		x	x		x		x	
Eli Lilly	**Follow-on Biologic**	12-2015	**Basaglar®**	**x**			**x**		**x**		**x**
Novo Nordisk	Therapeutic Equiv	6-2016	Levemir®	x		x		x			x
Novo Nordisk	Therapeutic Equiv	12-2016	Tresiba®	x		x		x			x
Sanofi	Therapeutic Equiv	2-2015	Toujeo®		x	x		x		x	

Other Biosimilars Approved Since August 2017

We have identified five other biosimilar approved by the FDA in the last half of 2017. Four have been delayed because of patent disputes, with one -- Humira, the #1 selling drug in the US -- being a controversial “pay for delay.”

FDA - Approved Biosimilars in 2017 Yet to Be Commercialized

FDA Approval	Biosimilar - Company	Incumbent - Company	Drug Class	Status
8/29/2017	Cyltezo - Boehringer	Humira - AbbVie	Autoimmune	patent disputes
8/30/17	Erelzi - Sandoz	Enbrel - Amgen	Autoimmune	patent disputes
9/14/17	Mvasi - Amgen/Allergen	Avastin - Roche	Cancers	patent disputes
9/16/17	Amjevita -- Amgen	Humira - AbbVie	Autoimmune	delayed until 2023 in return for settling patent disputes
12/14/17	Ixifi - Pfizer	Remicade - J&J	Autoimmune	no patent disputes but no plans to commercialize

On December 13, 2017 Pfizer announced that a second biosimilar to the J&J's incumbent Remicade was approved by the FDA. Given the failure of Pfizer's first biosimilar, it did not surprise us to see Pfizer announce that it had no immediate plans to commercialize this second biosimilar.

We have presented in more detail the price competition between Remicade and Inflectra in our recent paper Biosimilars and Exclusive Dealing Antitrust Law: The Case of Pfizer, Inc v Johnson & Johnson et al. We believe this experience will impact future biosimilar entry strategies pertaining to list pricing, rebate offers, and target markets.

In addition, It may increase "no go" decisions regarding biosimilars in the R&D pipeline and "pay for delay" agreements between biosimilars and incumbents.

While 2017 has been bad for the new biosimilar competitors, it has been good for competition as prices for incumbent drugs Remicade and Lantus have dropped significantly. Rather than argue for added legal and legislative protection for biosimilars, we argue for a rethinking of competitive strategy on the part of the entrants.

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