RISK strategies CONSULTING

WHITE PAPER

Developments and Considerations in the Biosimilar Landscape

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The biosimilar landscape has experienced significant evolution in recent years. In 2023, the blockbuster drug Humira, a specialty drug that is used to treat numerous inflammation related conditions including rheumatoid arthritis, Crohn's disease, and plaque psoriasis, had nine biosimilars launched. A distinct feature of the Humira biosimilar launch was the introduction of biosimilars for drugs under the pharmacy benefit, which deviates from historic launches of biosimilars primarily covered under the medical benefit. These biosimilars have proven to be just as safe and effective as Humira but are generally available at a much lower price point. This launch was anticipated to mark a pivotal moment in pharmacy, with the promise to offer more cost-effective alternatives for Humira, the top selling drug of all time.[1]

In recent months, Pharmacy Benefit Managers (PBMs) have been advertising the addition of multiple Humira biosimilars in a preferred status to their 2024 standard commercial formularies, while keeping Humira on the formulary with the same preferred formulary placement and utilization management requirements. However, making these biosimilars available by simply adding them to a formulary in the same preferred position as Humira will unlikely result in a significant market shift toward biosimilars.

These biosimilar strategies have raised concerns among plan sponsors and their consultants, who are questioning whether PBMs are maximizing the full savings potential of biosimilars by driving toward lowest-net cost alternatives, which is the lowest cost medication option after all discounts and rebates. While these concerns are valid, they do not always take into consideration the complex PBM environment, and the additional factors PBMs must weigh when developing such strategies.

In this white paper we will explore the history and evolution of biosimilars, dissect their competitive landscape and economic implications, and dive into recent 2024 PBM strategy announcements for Humira biosimilars. We will also examine the multifaceted challenges and opportunities associated with biosimilar competition and market penetration and analyze why these dynamics may influence short-term and long-term biosimilar strategies.

What is a Biosimilar?

Let's start with an overview explaining what biosimilars are and how they differ from generic drugs. A biosimilar is a biological product that is highly similar to and has no clinically meaningful differences from an existing reference (brand biological) product. In contrast to generic drugs which are identical replicas of brand drugs on an active ingredient basis, biologics are complex molecule drugs derived from living organisms. As a result, it is a challenge to achieve identical replication for biologics, therefore only similar drugs can be produced. Biosimilar manufacturers go through the FDA abbreviated review pathway which includes rigorous evaluation of molecular structure, and manufacturers must demonstrate there are no distinct differences in efficacy, safety, and quality compared to the reference product.[2]

History and Evolution

The Biologics Price Competition and Innovation Act (BPCI Act) went into effect in 2009 to provide the abbreviated review pathway which provides greater access to safe and effective biologics. The first biosimilar approved under the abbreviated pathway was Zarxio in 2015. There are now 45 biosimilars that have been FDA approved.[2]

Over the past eight years we have seen a significant evolution in biosimilar uptake, pricing, and strategy. Historically we have seen:

- Biosimilar discounts typically launch 10%-57% lower than the reference product[3]
- Biosimilars have entered the market for provider infused medications that are typically covered under the medical benefit
- Biosimilar manufacturers focused early research on oncology and immunology, with oncology leading the way in uptake in the first several years of biosimilar availability

The biosimilar landscape has evolved to:

- Increased competition driving aggressive discounts of up to 85% after six months post launch
- Biosimilars entering the market for drugs under the pharmacy benefit managed by PBMs such as biosimilars for Lantus and Humira, thus PBMs having influence to move market share more aggressively
- Research focused on oncology, autoimmune, and diabetes, with launches of biosimilars within the autoimmune class being the focus of 2023-2025

Pharmaceutical manufacturers have historically implemented their own strategies to maintain market share for their brand name reference products for as long as possible, even if that has meant lowering their costs or providing significant rebates to remain competitive. This practice allows continued profitability for the manufacturer, but also allows time for the manufacturer to influence physicians to transition the patient to an alternate or next generation drug which is still under patent within the same manufacturer's portfolio.

Manufacturers have also maintained market share by utilizing legal tactics to extend their patents, sometimes for many years beyond their original expiration date. A biosimilar cannot be launched if a manufacturer patent for the brand name is still active. Since the first FDA approved biosimilar in 2015, there have been several drugs that have had delayed launch dates relative to their FDA approval date. One such example of this is Amjevita, a biosimilar for Humira. Amjevita received FDA approval in 2016 but was unable to launch until seven years later in January 2023.

The biosimilar for Remicade, a provider infused drug typically covered under the medical benefit, was first FDA approved and launched in 2016. The manufacturer was able to retain market share of the reference product much longer than other biosimilars approved during that time, with only 13% of biosimilar penetration three years post launch. This was due to several reasons:

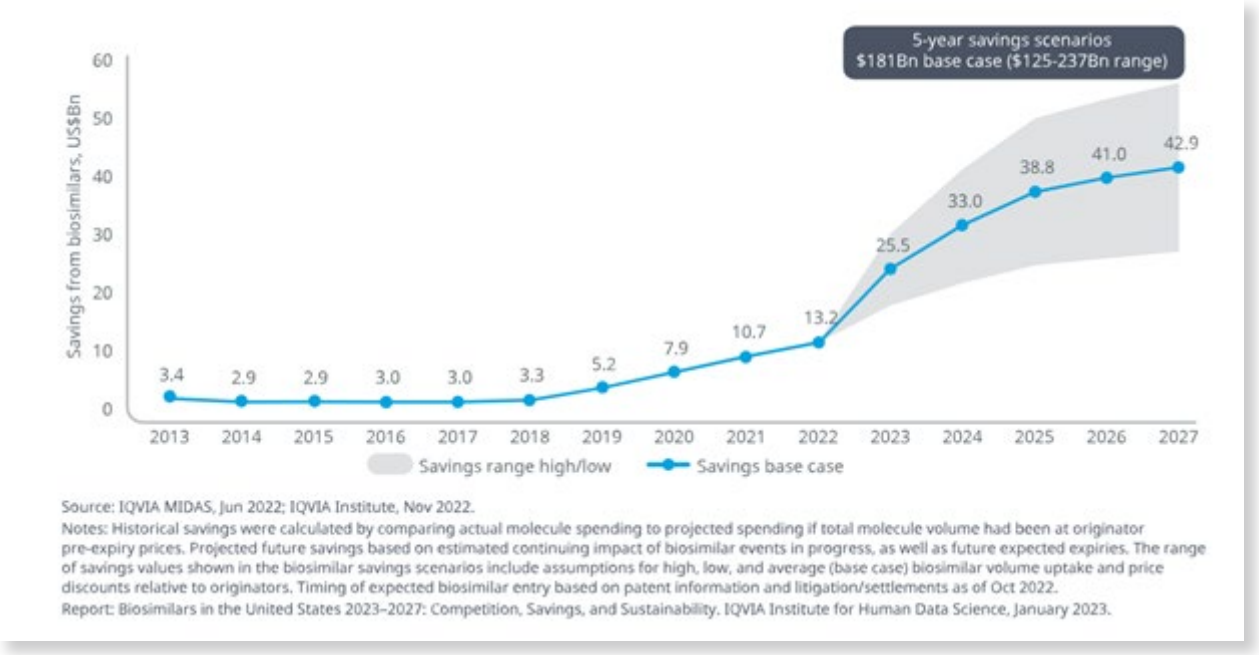
- A low number of biosimilar competitors (2) in early years
- Remicade was mostly covered under the medical benefit where management strategies have lagged in focus, strategy incentives, and controls compared to pharmacy benefit management
- Aggressive financial strategies by the manufacturer that provided incentives for providers to maintain reimbursement under buy and bill for Remicade
- Manufacturer exclusivity strategies to block competition of the drug[6]

While we have historical knowledge of biosimilar launches, each launch has had unique dynamics. Therefore, applying a standard biosimilar management strategy is not always the best approach and makes planning for future trends difficult to predict.

> Biosimilars are expected to reduce drug costs by **$181 billion** over the next five years.

Economic Value

Biosimilar competition has significantly contributed to decreased drug spend with an estimated $40 billion in cumulative savings over the past five years. With anticipated launches of some of the top spend drugs on the market and numerous competitors entering the market, biosimilars are expected to reduce drug costs by $181 billion over the next five years (2023-2027).[4]



Source: IQVIA MIDAS, Jun 2022; IQVIA Institute, Nov 2022.
Notes: Historical savings were calculated by comparing actual molecule spending to projected spending if total molecule volume had been at originator pre-expiry prices. Projected future savings based on estimated continuing impact of biosimilar events in progress, as well as future expected expiries. The range of savings values shown in the biosimilar savings scenarios include assumptions for high, low, and average (base case) biosimilar volume uptake and price discounts relative to originators. Timing of expected biosimilar entry based on patent information and litigation/settlements as of Oct 2022.
Report: Biosimilars in the United States 2023–2027: Competition, Savings, and Sustainability. IQVIA Institute for Human Data Science, January 2023.

Kaiser Permanente, the largest integrated delivery network, has historically been highly successful in driving biosimilar utilization, significantly outperforming the market due to its integrated influence. Their most recent success was the conversion of almost 90% of their commercial and Medicare members from Humira to the new biosimilar, Amjevita, and as a result, anticipate savings of $300 million in 2023.[5]

While the story of Kaiser's success with biosimilars offers hope, other areas of the healthcare system bring influence and complexity which doesn't always favor biosimilars as the sole option. The success of biosimilar competition in the long term relies on these alternatives gaining a significant market share. If they don't capture enough of the market, the value of investing in biosimilars research may decline and provide less motivation for manufacturers to bring future biosimilars to market.

Biosimilar Strategies in the Market: Focus on Humira

Our next section focuses on Humira biosimilars. In 2023, nine biosimilars for Humira, the top-selling drug in the world, were successfully launched.[1] Discount drug programs such as Mark Cuban's Cost Plus Drugs shook up the market in June 2023 by negotiating a biosimilar for Humira, named Yusimry, with a discount of 85% off of the Wholesale Acquisition Cost (WAC) of the reference product[7], a significant discount that had not been previously seen this soon after the original biosimilar launch. There are a few smaller PBMs, such as SmithRx, partnering with Mark Cuban's Cost Plus Drugs company to offer Yusimry at this high discount[8]. We anticipate specialty carveout PBMs such as Archimedes to continue to drive toward low WAC biosimilars.

All of the major PBMs (ESI, CVS Health, Optum, CarelonRx, Prime Therapeutics, and MedImpact) have announced their 2024 biosimilar strategy for their national commercial formularies. Each PBM will be adding varying biosimilar options, some at lower costs, while also keeping Humira on the formulary in a preferred formulary status.

In January 2024, CVS Health announced the removal of Humira from their major national commercial formularies starting April 1, 2024.* This will be the first large PBM to remove Humira from their commercial formulary and the company has estimated will bring up to 27% of savings to the autoimmune drug class.

Drug Name	Manufacturer	Pricing Strategy	WAC Discount	High Concentration	Citrate-free	Interchangeable
ESI National Preferred Formulary[10]						
Humira	Abbvie	n/a	-	●	●	-
Cyltezo	Boehringer Ingelheim (BI)	High-WAC	-5%		●	●
Hyrimoz	Sandoz	High-WAC	-5%	●	●	
adalimumab-adaz	Sandoz	Low-WAC	-81%	●	●	
CVS Standard Control Formulary[11]						
Humira*	Abbvie	n/a	-	●	●	-
Hyrimoz	Sandoz/Cordavis	High-WAC	-5%	●	●	
adalimumab-adaz	Sandoz/Cordavis	Low-WAC	-81%	●	●	
Optum Advantage Prescription Drug List[12]						
Humira	Abbvie	n/a	-	●	●	-
Amjevita	Amgen	High-WAC	-5%		●	
Cyltezo	BI	High-WAC	-5%		●	●
Hyrimoz	Sandoz	High-WAC	-5%	●	●	
adalimumab-adaz	Sandoz	Low-WAC	-81%	●	●	
CarelonRx Complete Drug List[13]						
Humira	Abbvie	n/a	-	●	●	-
Cyltezo	BI	High-WAC	-5%		●	●
adalimumab-abdm	BI	Low-WAC	-81%		●	●
Prime Therapeutics PrimeChoice Accord Formulary[14]						
Humira	Abbvie	n/a	-	●	●	-
Amjevita	Amgen	High-WAC	-5%		●	
Cyltezo	BI	High-WAC	-5%		●	●
MedImpact MedPerform Standard Formulary[15]						
Humira	Abbvie	n/a	-	●	●	-
Amjevita	Amgen	High-WAC	-5%		●	
Cyltezo	BI	High-WAC	-5%		●	●

Another unique biosimilar strategy emerging from CVS Health was in August 2023 when they announced their plan to enter into the drug manufacturer space, creating the company Cordavis that will co-produce and commercialize a portfolio of biosimilar products in the U.S Market.[16] The first biosimilar drug to be launched in 2024 by Cordavis will be a private label for the Humira biosimilar, Hyrimoz, and will be discounted more than 80% lower than the current list price of Humira. It is not a surprise that Hyrimoz is the preferred biosimilar on most of CVS Health's commercial formularies in 2024. This move shows CVS Health's efforts to align their business strategy with that of their clients to promote cost-effective biosimilar utilization, but also provides an alternate revenue stream for CVS Health which some have criticized.

What led to major PBMs keeping the reference product, Humira, on the formulary?

Risk Strategies Consulting spoke with several of the major PBMs regarding their 2024 biosimilar strategy for Humira, they noted some of the factors that were considered in evaluating their strategies. What seems like a straightforward decision is complicated by a number of factors, including:

- Manufacturer rebate influence
- Manufacturer market shift tactics
- Competition
- Regulation
- Interchangeability status
- Manufacturer capacity to produce adequate supplies of the product
- Pharmacy access and willingness to stock product
- The therapeutic uses, concentration, and formulation of the drug

Manufacturer assistance did not seem to be a factor as most biosimilar options have member copay assistance available to bring members' copay to $0.

Rebates

Rebates are primary revenue drivers for PBMs and can also be used to drive toward lowest net cost products for plan sponsors. Depending on plan sponsor contract terms regarding rebate sharing, a PBM may be incentivized to keep the reference product or the high WAC biosimilar on formulary instead of steering toward low WAC biosimilars, to ensure they are able to fund these guarantees. In some cases, the PBM may ask plan sponsors to change the terms of their contracts to allow for market share shift to the low WAC product, while not penalizing the PBM for not achieving previously negotiated rebate guarantees.

In addition, rebate yields are based on volume, so decreasing higher rebated drugs brings down the overall rebate yield, causing the PBM to make up those guaranteed dollars in other areas. Humira has been, and will likely continue to be, a highly rebatable drug. Significant market share, as well as rebates being tied to other top selling inflammatory drugs such as Skyrizi and Rinvoq complicates what lowest net cost means. In isolation, transitioning from Humira to its biosimilar in a straightforward conversion might appear to be the most cost-effective option. However, when considering the broader landscape, including the potential for Humira rebate improvement to compete with biosimilars and competition within the class, Humira may be able to remain competitive with biosimilars from a cost perspective.

Manufacturer Market Shift Tactics

As previously mentioned in the History and Evolution section, manufacturers of reference products will develop strategies to keep their share of the market for as long as possible. The manufacturer for Humira, AbbVie, also markets two of the top selling inflammatory competitors, Skyrizi and Rinvoq. The longer Humira has the market share the more time the manufacturer has to influence physicians to transition the patient to an alternate drug which is still under patent within the same manufacturer's portfolio. Conversely, if the PBM excluded Humira and preferred the biosimilars, the physician would have to write a new prescription for the biosimilar (due to lack of interchangeability status), and one could argue this could prompt the physician to write for a more expensive option such as Skyrizi or Rinvoq instead of the biosimilar; causing significant cost increase and accelerating the efforts of AbbVie to hold onto market share long term with an alternate product.

Competition

The biggest influence biosimilars have on driving down costs is the competition they bring to a previously dominated market. There are now nine biosimilars for Humira with varying methods of pricing strategies, concentration, formulation, and interchangeability status. There have been significant discounts on Humira biosimilars of 85% off of WAC in an unprecedented timeframe of six months. It appears AbbVie is aggressively trying to retain product market share for as long as possible, which could potentially drive out some of the competition over time.

As mentioned previously, pharmaceutical manufacturers need to be profitable to continue to invest in the biosimilar market. If biosimilars fail to gain sufficient market share, manufacturers will likely exit the market. If competition does subside, AbbVie could then increase the price of Humira, even without patent protection.

Risk Strategies Consulting also anticipates that the Inflation Reduction Act (IRA) will impact the future of biosimilar competition. The IRA allows the Centers for Medicare and Medicaid Services (CMS) to negotiate and set drug pricing for Medicare. While its primary objective is to lower drug prices, an unintended consequence is that fixed pricing will likely diminish the value proposition for manufacturers to invest in bringing new biosimilars to market, which would reduce competition. It is important to note that even though the IRA specifically addresses Medicare drug pricing, its repercussions will likely extend to other segments of the healthcare market. You can read more on the IRA impact to the healthcare system in our *Emerging Trends & Patterns in Healthcare Market Segments* white paper.

Interchangeability Status

Because a biosimilar is not an identical replica of the reference product, the FDA requires the manufacturer to go through additional testing to be designated as interchangeable. A designation of interchangeable means that a biosimilar can be substituted for a reference product by the dispensing pharmacy without prescriber's consent, state permitting. Only a handful of biosimilars on the market today have interchangeable status, and only two have been approved for interchangeability with low concentration Humira. Currently there are no interchangeable options for the high concentration Humira product which makes up over 85% of the market, creating a barrier for PBMs to be able to move market share smoothly without provider intervention. Teva's Alvotech was being reviewed for interchangeable status, and in April 2023 denied this status for the high concentration formulation, for the second time, with the FDA citing issues pertaining to quality shortfalls, subpar written records, problems with incoming stoppers and insufficient computer controls, among other manufacturing gaps.[9]

Manufacturer Capacity and Specialty Pharmacy Access

PBMs must investigate if manufacturers are equipped to provide reliable stock with increased demand in the case of the PBM limiting its offering to only a few preferred products. Drug shortages have become more significant in the past few years making this a consideration for PBMs. Additionally, PBMs must ensure specialty pharmacy networks are prepared, stocking enough inventory of biosimilars for the anticipated utilization demand, as well as aid in the conversion of Humira to biosimilar alternatives.

Summary and Assessment

Biosimilars hold the potential to offer more cost-effective treatments in high-cost drug categories by introducing competitively priced alternatives. The landscape of Humira, in particular, presents a significant opportunity for payors and plan sponsors to implement fresh strategies in managing both the utilization and cost for one of the top spend drugs of all time. Maximizing this cost-saving opportunity for plan sponsors is even more crucial given the recent unanticipated spikes in Glucagon-like peptide agonist (GLP-1a) (used to treat obesity and diabetes) utilization and spend, and the need to prepare for the financial impact of specialty drugs in the pipeline.

We explored numerous factors that contribute to the complex environment for PBMs when developing and/or executing a biosimilar strategy, though without full transparency it is difficult to conclude the most recent PBM biosimilar strategies are maximizing the savings opportunity of biosimilars. Adding to the complexity, PBMs are connected deeper into the supply chain than ever before, having incentives on the buy and sell side of the business, further hindering transparency and alignment in some cases. This significant biosimilar market event underscores the urgency for increased transparency and improved alignment between PBMs and their plan sponsors, something Risk Strategies Consulting has been promoting for several years.

Risk Strategies Consulting Pharmacy team is comprised of experienced clinical pharmacists and financial experts with deep industry knowledge of PBMs and the pharmaceutical supply chain. As leaders in negotiating fully transparent acquisition cost PBM arrangements, Risk Strategies Consulting stands at the forefront of driving the most cost-effective solutions for our clients. We advocate for clear communication of financial modeling, clinical management approaches, and market shift forecasting of biosimilar strategies to plan sponsors, providing them with comprehensive insights into these decisions and their impact on the cost-effectiveness of these drugs. Essential to achieve best price, transparency, and alignment, are contractual arrangements with PBMs possessing negotiating leverage, a commitment to negotiate true acquisition cost, full pass through of rebates and other forms of PBM remuneration, and formulary and clinical management optimization.

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