WHITEPAPER

Humira Biosimilars

Breaking Down the Hottest Topic in Pharmacy

Goodroot

Uncover what could happen with Humira and the biosimilar market in 2023

You've likely heard the big news: In 2023, several biosimilars for AbbVie's blockbuster anti-inflammatory drug, Humira, will enter the market. While biosimilars are intended to make notoriously expensive biologic drugs more affordable and accessible to patients, the reality is more nuanced.

This whitepaper explores the interesting history of Humira, the competitors expected to make their debut this year and our predictions for the future landscape within the autoimmune drug market.

These insights are brought to you through the collaboration of Goodroot and affiliate companies, RemedyOne and AlignRx, in partnership with Nuwae.

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About Goodroot

Goodroot is an interconnected community of companies making every interaction between human and health accessible, affordable and seamless. Goodroot's community, which includes AlignRx, Breez, CoeoRx, Emry Health, Penstock, RemedyOne, Sola and Nuwae — delivers transformative tech and proactive services that enable clients, partners and patients to reap more value from the money spent on health. We're laser-focused on holistically reinventing healthcare, one system at a time, to improve affordability and accessibility for patients. To date, we've removed over $1 billion in wasteful and unnecessary spending from the industry.

About AlignRx

AlignRx partners with pharmacy benefit consultants, employer groups, TPAs and health plans to offer pharmacy solutions and insights that improve performance, drive savings and deliver better outcomes across the pharmacy benefits value chain. Our robust Rx consulting team—made up of industry experts, data analysts and clinical pharmacists with decades of industry expertise and complete pharmacy landscape command—are in your corner year-round. We're ready to develop creative cost-containment opportunities, optimize your pharmacy spend and value, recover owed dollars and ensure PBMs are meeting contractual guarantees. Our PBM procurement process is the most meticulous in the industry, ensuring every important detail is accounted for within the contract.

About RemedyOne

RemedyOne is a formulary and rebate optimization company that cuts through the complexity that exists within modern pharmaceutical programs. Our clinically driven approach enables our team, which includes veteran pharmacists and an in-house Pharmacy and Therapeutics Committee, to assess new drugs, understand their cost and implications and make formulary recommendations based on research, insight and efficacy. We work with PBMs, health plans, employer groups and TPAs to provide clinical guidance and cost savings at every stage of the formulary and rebate management process.

In Partnership with Nuwae

Nuwae is leveling the playing field and changing the game when it comes to controlling the cost of prescription drugs. We believe that there should be one price for a drug, no matter who is paying. Our cutting-edge solutions are designed to lower the cost of prescription drugs by redeeming the tarnished "pharmaceutical rebate" into a force for good. We're solving the issues that drive drug prices to astronomical levels, ultimately lowering out-of-pocket costs and providing equitable access and outcomes for patients. Our mission is grounded in the belief that access to important medications should not be seen as a luxury or a benefit for select patients, and that no one should have to ration their medication due to cost.

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What are Biosimilars—are They Generics?

Biosimilars are not generics—they're not exact copies of their reference product but have the same clinical characteristics as their biologic originator product. Biologics are produced from living organisms which require a complex manufacturing process that cannot be replicated. Biosimilars go through an abbreviated Biosimilar Biologic License Application under the 351(k) biosimilar pathway.

History of Biosimilars

Increasing competition of originator products, through the introduction of potentially lower cost biosimilars, creates an opportunity to ease the financial burden associated with many specialty drugs. The passage of the Biologics Price Competition and Innovation Act (BPCI Act) in 2010 laid the groundwork for biosimilar approval by providing an abbreviated approval pathway for biosimilars. The approval process was slow moving in the beginning as only two biosimilars, Zarxio and Inflectra, were approved prior to 2017. Since then, approvals and uptake have been steadily increasing—with some biosimilars capturing significant market share within the oncology space.

Today—biosimilars seem to be the topic of conversation everywhere. Why? Humira. The launch of Humira biosimilars will be a test for industry stakeholders, as their entrance will reveal whether blockbuster drugs can be replaced to reduce the cost burden on payers.

History of Humira—A Timeline to Biosimilar Entrance

Figure A. Humira Timeline

2002	FDA Approval: AbbVie's Humira gains FDA approval for the treatment of rheumatoid arthritis. Its original formulation is a low concentration (50mg/ml).
2012	Humira becomes the top-selling drug in the world with $9.265 billion in global sales.
2016	Patent Expiration: AbbVie's Humira patent expires, and the company begins using litigation to potentially delay the launch of multiple FDA-approved Humira biosimilars.
2018	New Formulation: AbbVie launches a high concentration (100mg/ml) formulation of Humira—which reaches 85% of market share (only 6 out of the 14 projected biosimilars to Humira are high concentration).
2021	#1 Spot Retained for a Decade: Humira remains the top-selling drug in the world for 10 consecutive years with nearly $21 billion in global sales reported in 2021. After accumulating more than $200 billion in total revenue, AbbVie's Humira also holds the title of the world's all-time best-selling drug.
2022	Billions in Rebates: Through sizable rebates and contracts that limit competition, Humira has maintained the majority of market share after positioning itself in a preferred status on nearly every pharmacy formulary. AbbVie is expected to pay out approximately over $5 billion in Humira rebates for 2022.
2023	Market Opens to Biosimilars: Settlements with biosimilar manufacturers will finally allow market entrance of competitor products to begin.

Where We Are Today

Although the initial U.S. Humira patent expired in December 2016, AbbVie has used its patent portfolio (hundreds) and newer patents for the drug's manufacturing methods and formulations to gain over twenty years of exclusivity. In 2023, due to settlement agreements, exclusivity will end.

Many stakeholders within the industry are hopeful that biosimilars will increase competition and ultimately bring down the cost of specialty medications for autoimmune diseases. Historically, increased competition through the introduction of biosimilars has created opportunities to lower the financial burden associated with specialty drugs, which has reduced the risk for negative outcomes due to medication nonadherence. Because AbbVie's exclusivity has expired, biosimilar market entrance could eventually play a key role in impacting U.S. healthcare costs. But for that to happen, many of the barriers that exist, must be overcome.

Today—Humira—the number one selling drug in the world has the most extensive list of biosimilar candidates. In the following section, we'll introduce you to the new players—and discuss how they stack up.

Biosimilars to Humira—Meet the Players

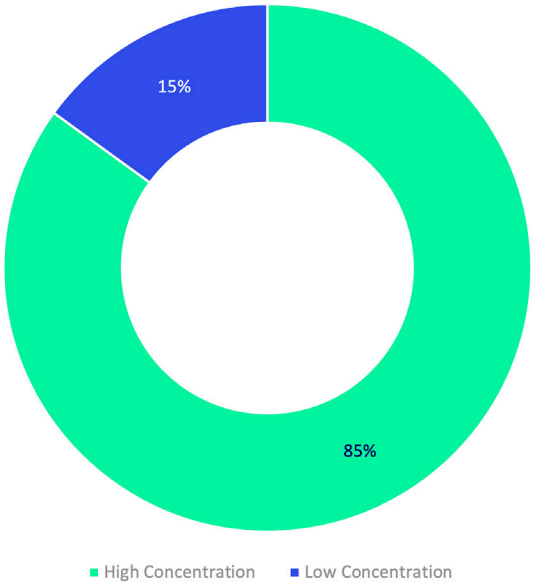
Ten manufacturers are expected to launch biosimilars to Humira in 2023—but how will they stack up to the world's all-time top selling drug? We compared the biosimilar hopefuls to AbbVie's Humira and here's how things are looking:

High Concentration Matters for Market Share

While most FDA-approved biosimilar products will launch in July 2023, Amgen's Amjevita, a low-concentration formulation, is slated to launch in early 2023.

The low concentration formulation only accounts for about 15% of the total Humira script volume, while the remaining 85% is the high concentration version. That's why true market penetration of any single biosimilar will likely only occur with a high concentration product.

Figure B. - Low vs. High Concentration Formulation and Script Volume



The Difference Between a High Concentration and Low Concentration Product

A high concentration product requires less volume to be injected, which can cause less injection site reactions and less pain. AbbVie shifted from the lower concentration to a higher concentration formulation to improve the patient experience. Doing so also prolonged its patent protection, resulting in more sales of Humira. Around 85% of all Humira prescriptions are now for the higher concentration formulation. Currently, only one high concentration formulation, Samsung Bioepis' Hadlima HC, has been approved by the FDA with an expected launch date in July 2023.

Citrate-Free Impacts Formulary Preferencing

AbbVie introduced citrate-free formulations of Humira in 2018 which allow for patients to experience less injection site pain and the use of a smaller needle. Aside from Sandoz's Hyrimoz and Samsung's Bioepis' Hadlima, all other FDA-approved biosimilar products will be available in citrate-free formulations, and this will also have some impact on formulary preferencing.

Figure C. Biosimilars to Humira: Approvals and Anticipated Launches

Biosimilar Name	Manufacturer	FDA Approval	Concentration	Citrate Free	Interchangeable	Anticipated Launch
Amjevita	Amgen	9/23/2016	Low (50mg)	yes	no	31-Jan-23
Amjevita HC (ABP 501 HC)	Amgen	Phase III	High (100mg)	yes	seeking	late 2023/ early 2024
Cyltezo	Boehringer Ingelheim	8/25/2017	Low (50mg)	yes	yes	1-Jul-23
Hyrimoz	Sandoz	10/30/2018	Low (50mg)	no	no	Jul-23
Hyrimoz HCF	Sandoz	pending (2023)	High (100mg)	yes	unknown	Jul-23
Hadlima	Samsung Bioepis/ Organon	7/23/2019	Low (50mg)	no	seeking	1-Jul-23
Hadlima HC	Samsung Bioepis/ Organon	8/15/2022	High (100mg)	yes	seeking	1-Jul-23
Hulio	Mylan/Biocon/ Viatris	7/6/2020	Low (50mg)	yes	no	Jul-23
Abrilada	Pfizer	11/15/2019	Low (50mg)	yes	seeking	1-Jul-23
Yusimry	Coherus BioSciences	12/17/2021	Low (50mg)	yes	no	1-Jul-23
Yusimry HC	Coherus BioSciences	ongoing clinical trials	High (100mg)	unknown	unknown	unknown
Yuflyma (CT-P17)	Celltrion	pending (2023)	High (100mg)	yes	seeking	1-Jul-23
Idacio	Fresenius	12/13/202	Low (50mg)	yes	no	1-Jul-23
AVT02	Alvotech/Teva	pending (2023)	High (100mg)	yes	seeking	1-Jul-23

Interchangeable Biosimilars

While all biosimilars are biologics that are just as safe and effective as an existing FDA-approved "reference product" or "originator," many Humira biosimilars are racing to gain interchangeable designation. But aside from Boehringer Ingelheim's Cyltezo—a low-concentration product, most Humira biosimilars do not have interchangeable designation. Many non-interchangeable biosimilars will launch and likely obtain interchangeability designation at a later date.

The Biologics Price Competition and Innovation Act (BPCIA), which was enacted in 2010, allows an interchangeability designation for FDA-approved biosimilars that meet the following additional requirements:

- Switching studies, in which patients alternate between the reference product and the interchangeable biosimilar, must reveal that the biosimilar product produces the same clinical result as the reference product
- The risk, in terms of safety or diminished efficacy of alternating or switching between use of the interchangeable biosimilar and the reference product, must not be greater than the risk of using the reference product without such alteration or switch

Biosimilars with interchangeable status do not require a patient's prescription to be changed by the prescriber ahead of time. Because pharmacy substitution is overseen at the state level, not at the federal level, it's up to the state laws and the state boards of pharmacy whether interchangeable substitution is allowed. If a biosimilar does not have interchangeable status, a new prescription from the provider is required.

Who allows interchangeable biosimilar substitutions?

Currently, 47 states and the District of Columbia allow pharmacists to substitute an interchangeable biosimilar without prior prescriber approval, but they must send a change notification to the prescriber within a specific timeframe. Notification to the patient before substitution with an interchangeable biosimilar is required in 40 states and the District of Columbia.

The Importance of Interchangeability

Interchangeability will likely be important from the perspective of a payer—who will want to have the least number of barriers to switch from Humira to a lower-cost biosimilar. Because an interchangeable biosimilar product will not require a new prescription from the prescriber, the payer could set up auto-substitution procedures with their contracted specialty pharmacies to accelerate the shift in market share. Interchangeable designation will not override formularies or PBM edits put in place to block the use of the biosimilars.

These high concentration biosimilars are all currently seeking interchangeability status:

1. Alvotech's AVT02
2. Amgen's Amjevita HC
3. Celltrion's Yuflyma (CT-P17)
4. Samsung Bioepis' Hadlima HC

The Use and Growth of Autoimmune Treatments

Humira, a TNF-alpha inhibitor, was an early player in the market and is used to treat a wide range of autoimmune diseases, including Rheumatoid Arthritis, Crohn's disease, Psoriasis, Psoriatic Arthritis, Ulcerative Colitis and Ankylosing Spondylitis. The use of autoimmune drugs is trending upwards, with a 10-15% increase year-over-year. Ulcerative Colitis treatments saw a 19% increase in utilization from 2021-2022.

How Humira Dominated the Autoimmune Market

- **Humira is versatile:** AbbVie's Humira has nine different indications, while other products typically focus on treatment within the Rheumatoid Arthritis and Psoriasis space.
- **Doctors prefer Humira:** Because Humira is often a first line—or preferred—treatment it's unlikely a doctor will switch a Humira-stable patient to another medication, regardless of the cost.
- **Rebate dollars add up:** The significant delta between the dollars for Humira and other existing products in the market makes it almost impossible for competitors to gain market accessibility.

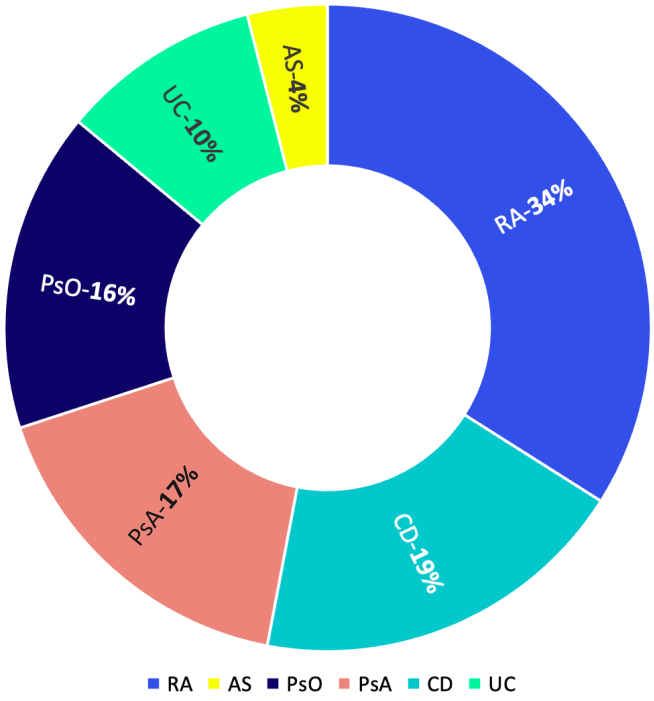


Figure D. Commercial Autoimmune Treatment Market Share by Indication

RA=rheumatoid arthritis; AS=ankylosing spondylitis; PsO=plaque psoriasis; PsA=psoriatic arthritis; CD=Crohn's disease; UC=Ulcerative colitis

**Source: Paid Claims data from February 2021– January 2022, AbbVie Inc.*

The Cost-Rebate Power Play

When it comes to cost, Humira is one of the most expensive autoimmune treatments available on the market—at a wholesale acquisition cost (WAC) of $83,328 annually (Figure E.). More affordable non-biosimilar drugs exist to treat autoimmune conditions—but the cost-rebate structure make them less favorable to the pharmacy benefit managers (PBMs) who control most formularies. Humira's rebate levels and high WAC pricing ensure that non-transparent PBMs are incentivized to prefer Humira over a drug like Kevzara as a first-line treatment for rheumatoid arthritis—which is priced lower and offers a smaller rebate.

Figure E. Autoimmune Treatments: Cost and Rebate Comparisons

RA=rheumatoid arthritis; AS=ankylosing spondylitis; JIA=juvenile idiopathic arthritis; PsA=psoriatic arthritis; PsO=plaque psoriasis; CD=Crohn's disease; UC=Ulcerative colitis; nr-axSpA=non-radiographic axial spondyloarthritis

Product	Manufacturer	Therapeutic Class	Route of Admin	RA	AS	JIA	PsA	PsO	CD	UC	nr-axSpA	2022 Annual Therapy Cost (WAC)
Humira (adalimumab)	AbbVie	TNF-alpha inhibitor	SQ	✓	✓	✓	✓	✓	✓	✓		$83,328
Enbrel (etanercept)	Amgen	TNF-alpha inhibitor	SQ	✓	✓	✓	✓	✓				$85,327
Cimzia (certolizumab)	UCB	TNF-alpha inhibitor	SQ	✓	✓		✓	✓	✓		✓	$66,296
Simponi SC (golimumab)	Janssen	TNF-alpha inhibitor	SQ	✓	✓		✓			✓		$72,438
Stelara SC (ustekinumab)	Janssen	IL-23/IL-12 antagonist	SQ				✓	✓	✓	✓		$55,329 (CD $165,731)
Skyrizi SC (risankizumab)	AbbVie	IL-23 antagonist	SQ				✓	✓	✓			$78,573 (CD $118,773)
Tremfya (guselkumab)	Janssen	IL-23 antagonist	SQ				✓	✓				$81,790
Ilumya (tildrakizumab)	Sun Pharmaceutical	IL-23 antagonist	SQ					✓				$66,596
Taltz (ixekizumab)	Eli Lilly	IL-17 antagonist	SQ		✓		✓	✓			✓	$81,546
Cosentyx SC (secukinumab)	Novartis	IL-17 antagonist	SQ		✓		✓	✓			✓	$84,127
Siliq (brodalumab)	Bausch Health	IL-17R antagonist	SQ					✓				$56,185
Actemra SC (tocilizumab)	Genentech/Roche	IL-6R antagonist	SQ	✓		✓						$55,954
Kevzara (sarilumab)	Sanofi/Regeneron	IL-6R antagonist	SQ	✓								$50,250
Orencia SC (abatacept)	Bristol-Myers Squibb	Immunosuppressant	SQ	✓		✓	✓					$65,894
Kineret (anakinra)	Swedish Orphan Biovitrum AB	IL-1R antagonist	SQ	✓								$62,192
Xeljanz (tofacitinib)	Pfizer	JAK inhibitor	Oral	✓	✓	✓	✓			✓		$63,287
Rinvoq (upadacitinib)	AbbVie	JAK inhibitor	Oral	✓	✓		✓			✓	✓	$69,000
Olumiant (baricitinib)	Eli Lily	JAK inhibitor	Oral	✓								$30,383
Otezla (apremilast)	Amgen	PDE4 Inhibitor	Oral				✓	✓				$52,854
Sotyktu (deucravacitinib)	Bristol-Myers Squibb	TYK2 inhibitor	Oral					✓				$74,998

Rebates Have Made Humira Untouchable

Because the “Big 3” PBMs: CVS Caremark, Express Scripts and OptumRx control an estimated 85% of all prescriptions in the United States, they bring billions in rebates from AbbVie each year. As a result of this recurring dynamic, Humira’s preferred placement on their formularies has been historically untouchable—and that will likely continue in 2023.

Formulary exclusions will also continue to occur in 2023. Bausch Health’s Siliq—a $56,185 drug used to treat Plaque Psoriasis is excluded from the top PBM formularies. Why? Though a significantly higher specialty rebate percentage is offered, it’s still less than the payout from the rebate offered by AbbVie for Humira. And Humira rebate contract requirements have provisions to limit a number of competitors, such as Siliq.

Figure F. Autoimmune Treatments: 2023 Formulary Management Comparisons

RA=rheumatoid arthritis; AS=ankylosing spondylitis; JIA=juvenile idiopathic arthritis; PsA=psoriatic arthritis; PsO=plaque psoriasis; CD=Crohn's disease; UC=Ulcerative colitis; nr-axSpA=non-radiographic axial spondyloarthritis

Product	Therapeutic Class	Route of Admin	OptumRx Premium Standard	CVS Caremark Standard Control	Express Scripts National Preferred	Humana Large Group	Prime Therapeutics Net Results	Indications
Humira (adalimumab)	TNF-alpha inhibitor	SQ	Preferred	**Preferred**	**Preferred**	**Preferred**	**Preferred**	**RA, AS, JIA, PsA, PsO, CD, UC**
Enbrel (etanercept)	TNF-alpha inhibitor	SQ	Preferred	**Preferred**	**Preferred**	Preferred	**Preferred**	**RA, AS, JIA, PsA, PsO**
Cimzia (certolizumab)	TNF-alpha inhibitor	SQ	Preferred	**Non-preferred**	**Preferred (nr-axSpA)**	Excluded	**Preferred**	RA, AS, PsA, PsO, CD, nr-axSpA
Simponi SC (golimumab)	TNF-alpha inhibitor	SQ	Preferred	Non-preferred	Non-preferred (UC)	Excluded	**Preferred**	**RA, AS, PsA, UC**
Stelara SC (ustekinumab)	IL-23/IL-12 antagonist	SQ	Preferred	Preferred	Preferred	Preferred	**Preferred**	**PsA, PsO, CD, UC**
Skyrizi SC (risankizumab)	IL-23 antagonist	SQ	Preferred	Preferred	Preferred	Preferred	**Preferred**	**PsA, PsO, CD**
Tremfya (guselkumab)	IL-23 antagonist	SQ	Preferred	Preferred	Preferred	Preferred	Preferred	**PsA, PsO**
Ilumya (tildrakizumab)	IL-23 antagonist	SQ	Excluded	Preferred	**Excluded**	Excluded	**Excluded**	**PsO**
Taltz (ixekizumab)	IL-17 antagonist	SQ	Non-preferred	Non-preferred	**Preferred**	Excluded	**Excluded**	**AS, PsA, PsO, nr-axSpA**
Cosentyx SC (secukinumab)	IL-17 antagonist	SQ	Excluded	Preferred	Excluded	Preferred	Preferred	**AS, PsA, PsO, nr-axSpA**
Siliq (brodalumab)	IL-17R antagonist	SQ	Excluded	**Excluded**	Excluded	**Excluded**	Excluded	PsO
Actemra SC (tocilizumab)	IL-6R antagonist	SQ	Non-preferred	**Non-preferred**	Non-preferred	Excluded	Preferred	RA, JIA
Kevzara (sarilumab)	IL-6R antagonist	SQ	Excluded	**Excluded**	Excluded	**Preferred**	**Preferred**	RA
Orencia SC (abatacept)	Immunosuppresant	SQ	Non-preferred	**Non-preferred**	Excluded	Excluded	Preferred	RA, JIA, PsA
Kineret (anakinra)	IL-1R antagonist	SQ	Excluded	**Non-preferred**	**Excluded**	**Excluded**	**Excluded**	RA
Xeljanz (tofacitinib)	JAK inhibitor	Oral	Preferred	**Preferred**	**Non-preferred**	Excluded	**Preferred**	RA, AS, JIA, PsA, UC
Rinvoq (upadacitinib)	JAK inhibitor	Oral	Preferred	**Preferred**	Preferred	Preferred	Preferred	RA, AS, PsA, UC, nr-axSpA
Olumiant (baricitinib)	JAK inhibitor	Oral	Excluded	Excluded	Excluded	Excluded	**Preferred**	**RA**
Otezla (apremilast)	PDE4 Inhibitor	Oral	Preferred	Preferred	Preferred	Preferred	Preferred	**PsA, PsO**
Sotyktu (deucravacitinib)	TYK2 inhibitor	Oral	Excluded	Excluded	Excluded	Excluded	Excluded	**PsO**

Figure G. Autoimmune Treatments: National Market Share

**Source: Paid Claims data from February 2019– January 2022, AbbVie Inc.*

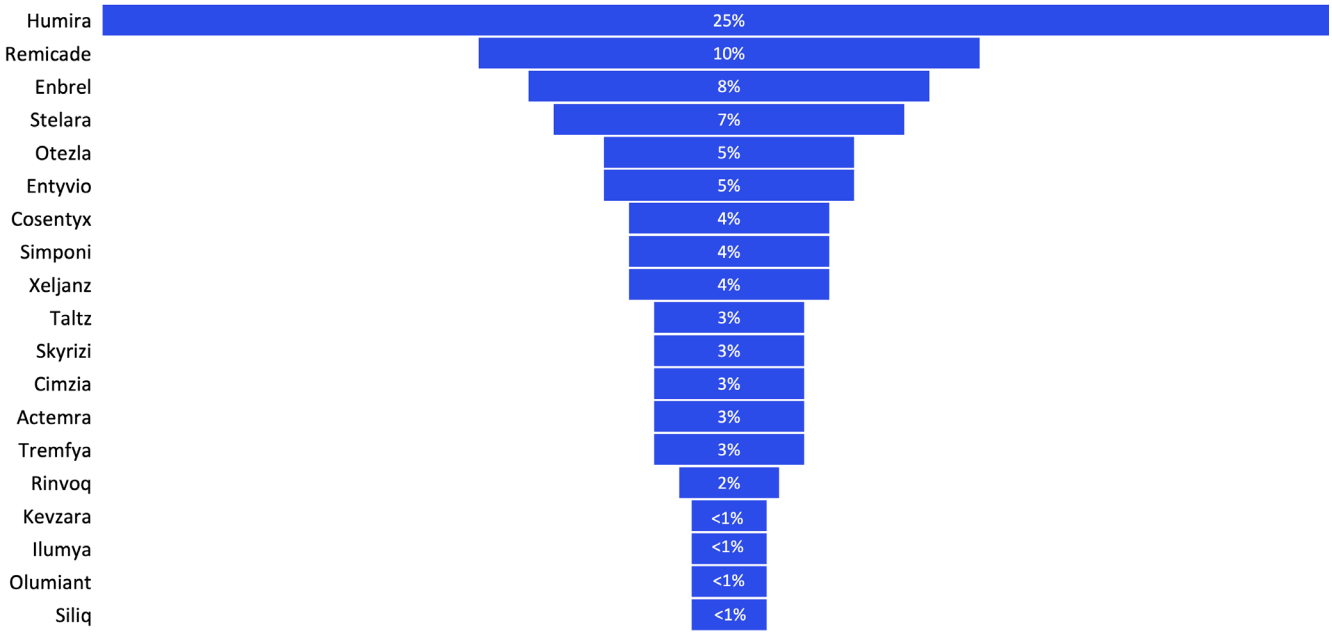


Figure H. Autoimmune Treatments: Approximate Annual Net Cost After Discount

** Wholesale Acquisition Cost (WAC) minus discounts*

Predictions on AbbVie Strategy for Humira Biosimilar Competition

AbbVie is well positioned to continue to shift brand utilization to their own products, Skyrizi and Rinvoq, in most of Humira's indications such as Ankylosing Spondylitis, Rheumatoid Arthritis, Psoriatic Arthritis, Psoriasis, Crohn's disease, and Ulcerative Colitis.

Having different mechanisms of action than Humira, both Skyrizi, an IL-23 antagonist, and Rinvoq, a JAK inhibitor, are often used in practice when there is a lack of response to TNF-alpha inhibitors such as Humira.

Expect AbbVie to Align Portfolio Incentives and Rebates to Increase

With the introduction of competing biosimilars into the market, AbbVie will likely increase their rebate above their current range for Humira's net cost after discount to remain competitive in the marketplace and retain preferred status on most PBM formularies. They will also likely increase rebates for Skyrizi and Rinvoq to maintain a preferred position for all three products on formularies.

AbbVie will likely continue to leverage their drug portfolio to provide additional incentives for placing all three of their products (Rinvoq, Skyrizi, and Humira) as preferred on the formulary and continue switching patients to these other products for specific indications.

Rebate Contract & Pricing Strategy

- AbbVie appears to be allowing a biosimilar in a preferred specialty position in their rebate contract, but they will NOT allow a member's out-of-pocket cost to favor the biosimilar, thus Humira will need to be tiered at the same preferred level as the biosimilars.

- By allowing the biosimilars to be co-preferred, there are strong indications that the net-cost differential between Humira and the biosimilars will either be neutral or may initially only slightly favor the biosimilars. AbbVie may respond by enhancing their rebate to neutralize the cost differential between their net cost after discounts and the biosimilar net cost after discounts.

- AbbVie has settled with all biosimilar competitors, allowing them to release their products and avoid further litigation—provided they follow specific conditions when launching their products. These settlement agreements include a royalty of the biosimilar company's net sales to be paid to AbbVie for various periods based on the individually held patents.

- It is likely the biosimilar manufacturers will initially be limited in their ability to price their product far below Humira due to the royalty fees that need to be paid to AbbVie.

- AbbVie offers copay cards and other resources, including the Humira Complete Care program, to patients taking Humira. Biosimilar manufacturers will need to offer these same services—which patients and prescribers have come to expect. It will be difficult for biosimilar competitors to discount their product enough when offering comparable programs.

The Big 3 PBMs—What They Do Matters to You

CVS Caremark, Express Scripts and OptumRx control an estimated 85% of Humira prescriptions in the U.S. They're in a unique and powerful position to dictate, or steer, the future of the market. It's likely that AbbVie will enhance rebate guarantees to minimize "Big 3" PBM movement toward biosimilar competitors.

Are any of the Big 3 ready to lose all—or a sizable portion—of their Humira rebates in favor of an all-biosimilar strategy?

Initially, no. Here are the top reasons why:

1. If Biosimilars come to the market with lower WAC, they cannot keep the same rebate-percent level as Humira as that would hurt negotiating GPO/large PBM's bottom line. PBMs and payers will lose a sizeable amount of revenue if they choose to prefer biosimilars over Humira.
2. Biosimilar manufacturers will need to have total (rebate + price) discount close to 75% of WAC to compete with Humira's current rebate (See Figure H).
3. AbbVie may increase its rebate by ~10% to ensure that the biosimilar manufacturers need to pay 55% to 85% total discount (rebate + price) and eliminate competition.
4. Abbvie may agree to GPO/large PBM demands to increase the Humira rebate %, allowing for an increase to PBM's per-claim guarantee to plan sponsors, to keep all happy and hinder biosimilar access (see Figure J).

Market share will depend on the economics dictated by Abbvie's Humira rebate contract in the marketplace. In the following pages, through illustrative economics, we analyze how biosimilar discounts and rebates could play out and effect market share.

Figure I. Example of Biosimilar Discounts and Rebate Modeling with Current Humira Rebate

**For illustrative purposes only*

Analysis I: Biosimilar Rebate % Needed to keep PBM Portion of Rebate Same as Humira Brand

Humira Brand Baseline	
Humira WAC	$6,944
Biosimilar price discount	0%
Product WAC	$6,944
Rebate %	32.00%
Rebate Paid by Manufacturer	**$2,222**
PBM Guarantee	$1,800
Patient copay coinsurance (5%)	$347
Plan sponsor net Cost	$4,797
PBM's portion of rebate	**$422**
Total discount (price+rebate)	**32%**

Biosimilar 10% lower WAC	
Humira WAC	$6,944
Biosimilar price discount	10%
Product WAC	$6,250
Rebate %	**35.50%**
Rebate Paid by Manufacturer	$2,219
PBM Guarantee	$1,800
Patient's copay coinsurance (5%)	$312
Plan sponsor net Cost	$4,137
PBM's portion of rebate	**$419**
Total discount (price+rebate)	**46%**

In this scenario, a biosimilar manufacturer with a 10% lower WAC would need to offer a 46% discount to keep PBM's rebate close to whole.

Biosimilar 20% lower WAC	
Humira WAC	$6,944
Biosimilar price discount	20%
Product WAC	$5,555
Rebate %	**40.00%**
Rebate Paid by Manufacturer	$2,222
PBM Guarantee	$1,800
Patient's copay coinsurance (5%)	$278
Plan sponsor net Cost	$3,477
PBM's portion of rebate	**$422**
Total discount (price+rebate)	**60%**

In this scenario, a biosimilar manufacturer with a 20% lower WAC would need to offer a 60% discount to keep PBM's rebate close to whole.

Biosimilar 30% lower WAC	
Humira WAC	$6,944
Biosimilar price discount	30%
Product WAC	$4,861
Rebate %	**45.50%**
Rebate Paid by Manufacturer	$2,212
PBM Guarantee	$1,800
Patient's copay coinsurance (5%)	$243
Plan sponsor net Cost	$2,818
PBM's portion of rebate	**$412**
Total discount (price+rebate)	**76%**

In this scenario, a biosimilar manufacturer with a 30% lower WAC would need to offer a 76% discount to keep PBM's rebate close to whole.

Figure J. Example of Biosimilar Discounts and Rebate Modeling with Humira Rebate Increase

**For illustrative purposes only*

Analysis II: Increase in Existing Humira Brand Rebate's Effect on Biosimilar Total Discount

If AbbVie decides to increase it's rebate, Biosimilar manufacturers would need to discount their products even further to keep the PBM whole. If the Humira rebate percentage increases to 40%, the PBM's portion of rebate increases from $422 to $978, making it even harder for biosimilar companies to match that dollar amount. For example, a biosimilar, offering a 10% lower WAC, would need to offer a total discount (rebate + price discount) of 55%. A biosimilar offering a 20% lower WAC, would need to offer a total discount (rebate + price discount) of 70%. A biosimilar offering a 30% lower WAC, would need to offer a total discount (rebate + price discount) of 87%. While plan sponsor net costs and patient copays would decrease in these scenarios, it would be nearly impossible for the biosimilar manufacturer to offer this type of discount.

Humira Brand	
Humira WAC	$6,944
Biosimilar price discount	0%
Product WAC	$6,944
Rebate %	**40.00%**
Rebate Paid by Manufacturer	$2,778
PBM Guaranty	$1,800
Patient's copay coinsurance (5%)	$347
Plan sponsor net Cost	**$4,797**
PBM's portion of rebate	**$978**
Total discount (price+rebate)	**40%**

Biosimilar 10% lower WAC	
Humira WAC	$6,944
Biosimilar price discount	10%
Product WAC	$6,250
Rebate %	**44.50%**
Rebate Paid by Manufacturer	$2,781
PBM Guaranty	$1,800
Patient's copay coinsurance (5%)	$312
Plan sponsor net Cost	**$4,137**
PBM's portion of rebate	**$981**
Total discount (price+rebate)	**55%**

Biosimilar 20% lower WAC	
Humira WAC	$6,944
Biosimilar price discount	20%
Product WAC	$5,555
Rebate %	**50.00%**
Rebate Paid by Manufacturer	$2,778
PBM Guaranty	$1,800
Patient's copay coinsurance (5%)	$278
Plan sponsor net Cost	**$3,477**
PBM's portion of rebate	**$978**
Total discount (price+rebate)	**70%**

Biosimilar 30% lower WAC	
Humira WAC	$6,944
Biosimilar price discount	30%
Product WAC	$4,861
Rebate %	**57.00%**
Rebate Paid by Manufacturer	$2,771
PBM Guaranty	$1,800
Patient's copay coinsurance (5%)	$243
Plan sponsor net Cost	**$2,818**
PBM's portion of rebate	**$971**
Total discount (price+rebate)	**87%**

Effect of Humira Rebate Increase Plus PBM Per Claim Guaranty Increase for Humira

Humira WAC	$6,944
Biosimilar price discount	0%
Product WAC	$6,944
Rebate %	**40.00%**
Rebate Paid by Manufacturer	$2,778
PBM Guaranty	**$2,200**
Patient's copay coinsurance (5%)	$347
Plan sponsor net Cost	**$4,397**
PBM's portion of rebate	**$578**
Total discount (price+rebate)	**40%**

Humira WAC	$6,944
Biosimilar price discount	0%
Product WAC	$6,944
Rebate %	**42.00%**
Rebate Paid by Manufacturer	$2,916
PBM Guaranty	**$2,400**
Patient's copay coinsurance (5%)	$347
Plan sponsor net Cost	**$4,197**
PBM's portion of rebate	**$516**
Total discount (price+rebate)	**42%**

Humira WAC	$6,944
Biosimilar price discount	0%
Product WAC	$6,944
Rebate %	**44.00%**
Rebate Paid by Manufacturer	$3,055
PBM Guaranty	**$2,500**
Patient's copay coinsurance (5%)	$347
Plan sponsor net Cost	**$4,097**
PBM's portion of rebate	**$555**
Total discount (price+rebate)	**44%**

If you're a payer, it's also important to note that if AbbVie increases it's rebate percentage (and your PBM is receiving a larger portion of that rebate), you should be asking for a higher guarantee. For example, if AbbVie raises its rebate rate (e.g. 40%) to the PBMs, and your guarantee from the PBM is $1800, you should receive an increase in your guarantee from $1800 to $2200 from your PBM.

Predictions on Shift in Market Share from Humira to Biosimilars

Our detailed analysis of multiple biosimilars for Humira set to enter the market in 2023, find that the downward pressure on drug cost will be minimal, at least initially. We see Humira biosimilars potentially capturing up to 5 percent market share in the first year, and reaching a maximum of 20-25 percent by 2026.

**These predictions are based solely on our expertise and pharmacy command and are subject to change.*

Potential Payer Strategies for Biosimilars to Humira

1. Offer both Humira and biosimilars at parity

Some payers will continue to take a Humira rebate, allow access to lower cost biosimilars, and negotiate rebates with the biosimilar manufacturers. Both OptumRx and Express Scripts have already opted for this strategy—and this will most likely be the leading strategy, given the concessions AbbVie has already made in contracting to allow both brand and biosimilars to coexist.

2. Prefer biosimilars and disadvantage Humira

Payers have the option to give up the Humira rebate and choose a biosimilar product with a lower net cost. While this is less likely, integrated health plans may be able to shift market share to lowest cost biosimilars. A true low net-cost formulary might only prefer the biosimilar(s) with the lowest cost and disadvantage the other biosimilars, along with Humira.

3. Prefer Humira and disadvantage biosimilars

Other payers may continue to take Humira rebate and block access to lower cost biosimilars. This is the least likely option and too fraught with potential higher out-of-pocket costs for patients.

Which biosimilar products to prefer will be dependent upon the following:

- Concentration (high vs. low)
- Citrate-free formulation
- Interchangeability status
- Pen-injector availability
- Manufacturer reputation
- Manufacturer rebates
- Net cost
- Supply-chain stability

Next Steps for Industry Stakeholders

Health Plans and Employer Groups

Starting now, payers should continually review their product positioning and rebates in the autoimmune class as this class represents most specialty rebates and overall specialty cost. Sophisticated data analysis is required to ensure that the appropriate products, in the appropriate access positions, and at the lowest net cost, are available to patients.

Payers who have rebate-guarantee contracts with PBMs should ensure that their specialty-rebate guarantee is increased in cases where Humira remains as a formulary preferred brand and other brand products are renegotiated for higher rebates.

Biosimilar Manufacturers

Initially, biosimilar manufacturers will likely compete with other biosimilar manufacturers, and not with AbbVie's Humira. They will want to ensure profit and a preferred formulary position as not all biosimilars will be added. How? It will likely require a biosimilar to give up more rebate dollars—which should lead to increased market share. In the future, when the time comes to eliminate Humira from preferred position, a previously preferred biosimilar is in a better position to capture the Humira market share that will be up for grabs.

Pharmacy Benefit Managers (PBMs)

The balancing act for PBMs will likely require the continued use of Humira rebates and the inclusion of lower WAC biosimilars. To meet the needs of their clients, and satisfy their own business interests, the PBM will need to carefully select and promote biosimilar products that will help lower net costs, beyond Humira—within the guardrails of their Humira rebate contract. Eventually, payers and PBMs (of all sizes) will want to ensure their Humira market share is at or below the national shares, so that when and if the Big 3 PBMs decide that Humira should no longer be a preferred drug (and AbbVie reduces or eliminates the Humira rebate) that the increased cost for the remaining market share of Humira can be absorbed by the lower net costs of the collective biosimilar market shares.

Patients

In some instances, when Humira and a biosimilar are on the same formulary tier, patients should view biosimilars as an opportunity to lower their out-of-pocket costs without sacrificing clinical efficacy. Depending on coinsurance, deductibles, and out-of-pocket maximums, a lower unit price biosimilar could result in lower patient costs.

Brokers & TPAs

While the biosimilars coming to market are expected to be more affordable than Humira, broker and TPA clients likely won't see a huge reduction in unit cost. Larger savings will come in the form of rebates. However, PBMs often have standard exclusion language where they exclude biosimilars from pricing guarantees. That's why it's important to have a partner who can scrutinize contract details and potentially renegotiate contracts to include biosimilars.

While biosimilars may eventually pave the way for less expensive alternatives to an entire class of complex and costly drugs—the following proven cost-containment pharmacy solutions are available to your clients right now:

- International filling
- Income-based funding solutions
- Copay assistance
- Manufacturing assistance
- Step therapy
- Prior authorization
- Quantity limits

Conclusion

In 2023, we expect to see 12 biosimilar products enter the market and compete with AbbVie's Humira. Given the cost-rebate power play—and the monetary loss that PBM stakeholders and health plans assume when rebate dollars are removed—we don't anticipate any significant shift to biosimilars or cost savings as Humira biosimilars become available. While market share for autoimmune treatments has historically been dominated by Humira, competition will largely depend on the economics dictated by AbbVie. If they increase their rebate, it will be nearly impossible for biosimilars to make the cost impact that many are hopeful for. But there may be a tipping point in biosimilar pricing where the net cost differential will be significant enough to force payers to make their PBMs prefer the biosimilars. Biosimilars net-priced at 50% or more might be that tipping point. However, this significantly lower net price must be coupled with a significant shift in market share to make up for the loss of Humira rebate.

Definitions

Biologics:

Biologics are large, complex molecules that are manufactured from living organisms

Originator:

Also called a reference product, an originator is an FDA-biologic drug that biosimilars are modeled after

Biosimilars:

A biologic that is just as safe and effective as an existing FDA-approved biologic, also referred to as the “reference product” or “originator”

Interchangeable:

Interchangeable product is one that may be substituted for the reference drug by a pharmacist without the intervention of the healthcare provider who prescribes the product. For an interchangeable product, beyond demonstrating that the products are biosimilar, there are additional statutory standards that need to be met.

For a biosimilar product, if a patient takes their prescription to a pharmacy, their prescription would be filled with exactly what is written. For an interchangeable product, if a patient takes their prescription to a pharmacy, their prescription may be filled with the reference product, or may be filled with the interchangeable product. Pharmacy substitution is overseen at the state level, not at the federal level, so it’s up to the state laws and the state boards of pharmacy whether interchangeability is allowed.

Generics:

Manufactured from small-molecule, chemical compounds that can reliably and identically be reproduced the minute a brand drug’s patent expires.

WHITEPAPER

Humira Biosimilars — Breaking Down the Hottest Topic in Pharmacy

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