GENERICS BULLETIN
CITELINE COMMERCIAL

June 23, 2023 | **Analysis**

Generics Bulletin Explains: The Next Wave of US Humira Biosimilars

Start of July Will See an Explosion of Competition in Adalimumab in US from 8 Rivals

by David Wallace

Following Amgen's debut of the first US Humira rival earlier this year, as many as eight further FDA-approved adalimumab biosimilars are about to launch. *Generics Bulletin* breaks down all the different players and how they are positioning themselves in such a competitive market.

Anyone with even a passing interest in the global off-patent industry will likely be aware of the significance of 2023 for the US biosimilars market.

Humira – for a long time the world's top-selling drug, and still one of the biggest brands in the business – finally faced US biosimilar competition this year, with Amgen at the end of January launching the first of many adalimumab biosimilars that have been approved by the US Food and Drug Administration.

But while that milestone has now been passed, an arguably even more significant development looms on the horizon.

Because around the end of June and the start of July, a multitude of other competitors will be bringing further

FDA-approved adalimumab biosimilars

Amgen's Amjevita (adalimumab-atto)

Biocon's Hulio (adalimumab-fkjp)

Boehringer Ingelheim's Cyltezo (adalimumab-adbm)

Celltrion's Yuflyma (adalimumab-aaty)

Coherus's Yusimry (adalimumab-aqvh)

adalimumab biosimilars to the US market, as per the terms of their individual litigation settlements with originator AbbVie. (Also see "*Humira In 2023: The $17bn Biosimilar Opportunity*" - Generics Bulletin, Jan. 5, 2023.)

This will kick off a period of fierce competition in the back half of the year that will see developers seek every opportunity to gain an advantage over their rivals as they jockey for position in such an unprecedentedly competitive situation for biosimilars.

Fresenius Kabi's Idacio (adalimumab-aacf)

Pfizer's Abrilada (adalimumab-afzb)

Samsung Bioepis/Organon's Hadlima (adalimumab-bwwd)

Sandoz's Hyrimoz (adalimumab-adaz)

With so many launches of biosimilars of the same molecule coming in such a short space of time, *Generics Bulletin* looks at the various players in the adalimumab market and how they are seeking to differentiate their offering.

The First To Market

Amgen's Amjevita (adalimumab-atto) undoubtedly began with the greatest advantage, in the form of a five-month head-start over its closest biosimilar competitors.

Launching on the final day of January, Amjevita was made available at a list price or wholesale acquisition cost that was 55% below Humira's brand price, or alternatively at a list price 5% below that of Humira. (Also see "*Amgen Delivers On Launch Of First US Humira Rival – At A 55% Discount*" - Generics Bulletin, Jan. 31, 2023.)

Amgen subsequently explained that this was "to provide broad access for patients by offering two options to health plans and pharmacy benefit managers," as part of efforts to "address the complexity of the US market." (Also see "*Amgen Talks Dual Pricing Strategy For Amjevita*" - Generics Bulletin, Feb. 1, 2023.) Undisclosed rebates would play a major role for the 5%-cheaper version, Amgen acknowledged.

Initial Q1 figures revealed by the company showed that in its first two months on the market, Amjevita generated turnover of $51m, with a majority of sales "related to inventory build," according to the company. (Also see "*Amgen Reveals First Figures For US Humira Rival*" - Generics Bulletin, April 28, 2023.)

While Amgen cautioned against being able to maintain this sales level in future quarters – "looking ahead, we expect Q2 Amjevita sales in the US to be lower than Q1 sales," management acknowledged – the firm said it was nevertheless "encouraged by the high awareness of Amjevita

among gastroenterologists and rheumatologists."

The Interchangeable Biosimilar

One factor that is seen as potentially influencing uptake for Humira biosimilars is interchangeability. The FDA's interchangeability designation allows pharmacists to substitute a biosimilar for its reference biologic without consulting the original prescriber, subject to state law – and adalimumab's presence in the retail channel makes this aspect particularly pertinent. (Also see "*Cutting Through The Confusion On US Biosimilar Interchangeability*" - Generics Bulletin, Aug. 5, 2022.)

So far, the only adalimumab biosimilar to be approved as interchangeable with Humira is Boehringer Ingelheim's Cyltezo (adalimumab-adbm), which was granted the interchangeability designation in late 2021. The company referred to the achievement as "a true milestone and an important step forward for broader adoption in the US and for patient access to affordable medicines" (*see sidebar*).

First Interchangeable Humira Biosimilar Approved In US

By David Wallace

18 Oct 2021

Boehringer Ingelheim has won a landmark first US interchangeability designation for a biosimilar to Humira, with the firm's Cyltezo version of adalimumab representing the second ever interchangeable biosimilar approved by the FDA.

Read the full article here

The other biosimilar that had been expected to be able to compete at launch with an interchangeability designation is Alvotech's AVT02 candidate, which references the 100mg/ml higher-concentration version of Humira – unlike Cyltezo, which is based on the original 50mg/ml version. (Also see "*Alvotech Humira Settlement Sets Up Interchangeable Adalimumab Showdown*" - Generics Bulletin, March 9, 2022.)

However, Alvotech has faced a series of setbacks as it attempts to gain approval for its adalimumab biosimilar, in the form of multiple complete response letters from the FDA linked to inspections of its Reykjavik plant. As such, the firm's ability to gain FDA approval before the potential launch date of 1 July is now in question, with the most recent potential action date provided by the agency being June 28. (Also see "*Alvotech's Latest FDA Knockback Cuts It Fine For Humira Rival*" - Generics Bulletin, April 14, 2023.)

Further interchangeability designations for other versions of adalimumab are also in the works from other biosimilar developers, but they will have to wait until any exclusivities expire before they can be marketed as such, as FDA rules grant first interchangeable biosimilars a year of market exclusivity.

GENERICS BULLETIN
CITELINE COMMERCIAL

The High-Concentration Versions

While Alvotech is still awaiting approval for its high-concentration adalimumab biosimilar, three other 100mg/ml biosimilars have already been approved by the FDA – two of which are also approved in 50mg/ml presentations.

The first company to obtain FDA approval for a higher-strength Humira biosimilar was Samsung Bioepis, for its Hadlima (adalimumab-bwwd) version. (Also see "*Samsung Bioepis And Organon Get First High-Concentration Adalimumab Nod In US*" - Generics Bulletin, Aug. 17, 2022.) The August 2022 approval for the biosimilar – which will be marketed by Organon – follows approval for Hadlima as a 50mg/ml formulation back in July 2019. (Also see "*Samsung Bioepis Gets US Adalimumab Nod*" - Generics Bulletin, July 24, 2019.)

Organon believes its July 1 launch will benefit from being able to offer both strengths of adalimumab, as well as considerable real-world evidence from launches of Hadlima in other global markets, along with an ergonomic pen design. However, the firm has set expectations only for a "modest ramp" in sales this year, "with the market for biosimilars really forming in 2024 to 2025" (*see sidebar*).

Organon Tempers Expectations Ahead Of Adalimumab Second Wave

By David Wallace

09 May 2023

Ahead of joining a second wave of Humira biosimilars hitting the US market in just a couple of months, Organon has projected a "modest ramp" in initial sales for its Hadlima version in 2023.

Read the full article here

The second firm to gain approval for a high-concentration adalimumab biosimilar was Sandoz, which in March this year announced the FDA nod for its Hyrimoz (adalimumab-adaz) version. (Also see "*Sandoz Gains An Edge With High-Concentration US Humira Biosimilar*" - Generics Bulletin, March 22, 2023.)

Sandoz CEO Richard Saynor was candid, however, that with so many biosimilars competing for placements with only three major payers, "I have no idea" what's going to happen. "Clearly the originator is going to do everything it can to either bundle or maintain as much share as possible," Saynor suggested. "So I'm relatively cautious in terms of my expectations. We'll see what happens." (Also see "*Sandoz Chief Looks To Build On Recent Deals*" - Generics Bulletin, March 2, 2023.)

And the third FDA approval for a 100mg/ml adalimumab biosimilar came relatively recently, for Celltrion's Yuflyma (adalimumab-aaty), which is not approved in a 50mg/ml format. (Also see "*Celltrion Bags FDA Approval For High-Concentration Humira Rival*" - Generics Bulletin, May 25, 2023.)

The Celltrion product will be one of the first biosimilars to be marketed by the Korean firm in the US directly, rather than through partnerships. (Also see "*Building A US Business: Celltrion's New CCO Talks Strategy*" - Generics Bulletin, March 28, 2023.)

The Big Pharma Clout

One aspect that could prove to be a deciding factor in the US adalimumab market is the size and strength of the organization marketing each biosimilar.

While Amgen has already launched its version, another major pharma industry giant in the race for biosimilar Humira is Pfizer, which won approval for its Abrilada (adalimumab-afzb) product in late 2019. (Also see "*Pfizer's FDA-Approved Adalimumab Faces Four-Year Wait*" - Generics Bulletin, Nov. 18, 2019.)

Although the company has been relatively quiet on biosimilars in recent months – despite bringing in more than $2bn in biosimilars sales in 2022 (Also see "*Pfizer Quietly Chalks Up Another $2bn Year For Biosimilars*" - Generics Bulletin, Feb. 8, 2023.) – the firm is still very much focused on the opportunity offered by Abrilada.

Pfizer is seeking to eventually obtain an interchangeability designation for its biosimilar (Also see "*FDA To Review Pfizer's Abrilada For Humira Interchangeability*" - Generics Bulletin, March 3, 2022.), and has indicated that it expects to gain a "fair" share of the adalimumab market once it launches. (Also see "*Pfizer Anticipates 'Fair' Share Of Adalimumab Market In US*" - Generics Bulletin, May 5, 2022.)

Analysts seem to agree. Around the time of the Amjevita launch at the end of January this year, Truist Securities predicted that as the adalimumab market plays out, "Amgen and Pfizer will likely own the largest market shares with Coherus potentially grabbing a piece of the pie later." (Also see "*Adalimumab Expectations Revised In The Wake Of Amgen Launch*" - Generics Bulletin, Feb. 1, 2023.)

Competing Aggressively On Price

Talking of Coherus, the firm recently made waves with a major announcement that delivered on hints previously dropped by the firm that it intends to compete aggressively on price in the adalimumab market.

Back when Coherus obtained FDA approval for its Yusimry (adalimumab-aqvh) biosimilar in late 2019, the company promised that its launch would be accompanied by a "compelling value proposition." (Also see "*Coherus Promises 'Compelling Value Proposition' After US Adalimumab Approval*" - Generics Bulletin, Dec. 20, 2021.)

And recently, competitors found out exactly what that meant when Coherus announced that it

GENERICS BULLETIN
CITELINE COMMERCIAL

would be selling Yusimry at a massive 85% discount to Humira, as well as partnering with Mark Cuban's Cost Plus Drugs company to sell the biosimilar at an even steeper discount (*see sidebar*).

The move was so significant that it apparently led AbbVie to conclude that it violated the terms of its settlement agreement with the biosimilar developer, launching legal action against the firm in the face of Coherus' denials. (Also see "*Coherus And AbbVie Trade Legal Blows Amid Radical Adalimumab Price Offering*" - Generics Bulletin, June 15, 2023.)

Whether other biosimilars can compete effectively at these kinds of discounts remains to be seen, but other players in the market have so far shown few signs of being deterred.

Coherus Plots 'Lowest Price Adalimumab' With Huge Discount, Ties Up With Mark Cuban

By Dean Rudge

June 1, 2023

Coherus BioSciences had teased a "compelling value proposition" for its Yusimry (adalimumab-aqvh) biosimilar to AbbVie's Humira blockbuster and it has delivered, with a pair of pricing strategies include one though an alliance with self-labelled "disruptor" Mark Cuban.

Read the full article here

Biocon recently pointed to "strong interest" in its upcoming US launch of Hulio (adalimumab-fkjp), backed up by the product's previous performance in Europe. The Indian firm – which recently bought out the biosimilars business of former partner Viatris – said it was "very confident" about its "four channel strategy" in the US – from payers to prescribers to specialty pharmacies and the end patient – promising that "you'll see a tremendous amount of interest with our Hulio product as we progress."

Biocon also hinted that it would adopt both a branded and unbranded strategy, marketing its biosimilar "either on the high rebate side or on the low side from a WAC standpoint because we will have our Hulio branded product and we'll have the authorized [version] that would be the adalimumab." (Also see "*Biocon Pumps Up For Adalimumab US Debut Amid Payer 'Steady State'*" - Generics Bulletin, June 1, 2023.)

Meanwhile, Fresenius Kabi – a relatively new player in US biosimilars – has suggested that reliability in supplying the market will be a chief concern for customers as it prepares to launch its Idacio (adalimumab-aacf) version.

Ultimately, senior vice president for US biosimilars Ali Ahmed told *Generics Bulletin* earlier this year, adalimumab customers "want to see that long term sustainability from manufacturers. As such, when we speak to customers, that's why we highlight our investments in supply, supply

reliability, and manufacturing capabilities."

"We have a very strong track record in terms of our supply and manufacturing capabilities in the US," he added. "And I think that resonates with customers and key stakeholders, because the first thing they want to know is, 'If we are going to adopt a product, how reliable will you be in supplying the market?'"

"With chronic conditions, supply is fundamentally important to build their confidence. That is, at least for us, probably the thing that has been really resonating with our key stakeholders." (Also see "*Fresenius Kabi: Adalimumab Customers Want Supply Guarantee, We Can Provide That*" - Generics Bulletin, Jan. 25, 2023.)

Limited Spots Available On PBM Formularies

One factor that will be crucial in enabling access and uptake for adalimumab biosimilars is securing inclusion on the formularies of pharmacy benefit managers.

Last year, United Health Group's in-house pharmacy benefit manager Optum Rx indicated that it plans to include up to three Humira biosimilars on its formularies in 2023, beginning with the first one that becomes available. (Also see "*Optum Rx Reveals Humira Biosimilar Plan To 'Support Advancement Of The Market'*" - Generics Bulletin, Dec. 2, 2022.)

Meanwhile, Cigna – owner of Express Scripts – in late 2022 announced that it would "add biosimilars as preferred products on its commercial formularies at the same position as Humira" as they become available.

And Prime Therapeutics also announced early this year that it would "begin recommending Humira biosimilars to sit alongside Humira in the inflammatory drug class on its preferred list of drugs."

However, details are still thin on the ground in terms of which biosimilars will be prioritized by the PBMs.

In terms of predictions for how the shape of competition to Humira will play out over the next few quarters, one of the best people to ask may be originator AbbVie, which predicted with a high degree of accuracy the impact of biosimilar competition in Q1.

AbbVie Sets Biosimilar Expectations As It Prepares To Take The Plunge On Humira

By David Wallace

Feb. 10, 2023

AbbVie has set out its expectations for US biosimilar competition to Humira this year,

AbbVie reported US Humira revenues that were down by a little over 26% in the first quarter, in line with the originator's earlier forecast of 27% erosion. And the firm is expecting 27% sales erosion in the US for Humira in Q2.

But "with one biosimilar currently in the market and potentially nine more biosimilars available in the middle of the year, we anticipate that sales erosion will be more heavily weighted towards the second half of 2023," the firm has predicted (*see sidebar*).

For 2023 as a whole, AbbVie has predicted 37% erosion in the US, a figure that falls towards the lower end of an earlier guidance range that had been provided of 35%-55%.

"Really in the first half of the year the vast majority of that erosion will be price," the firm described.

Then "in the second half, because we've contracted rebates, you'll see a step-up in the price erosion, although you also will see more volume; with [up to] nine biosimilars coming to the market in the middle of the year, we would expect a little bit more volume erosion."

And looking further ahead, AbbVie management suggested that "as we think about 2024, we would expect based on the contracts to see a step-up in price, albeit not at the same level as we see in 2023, but 2024 would be more volume. It's probably the best way to think about it right now."

predicting 37% brand erosion with pressures ramping up in the second half of 2023 as Amgen's Amjevita is followed into the market by numerous other adalimumab rivals. Management also commented on pricing dynamics after Amgen offered a dual-discount strategy.

Read the full article here