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Humira In 2023: The $17bn Biosimilar Opportunity

Landmark LOE Looms In US; Several Adalimumab Launches Expected Throughout Year

by David Wallace

The advent of US biosimilar competition to Humira in 2023 represents the largest ever loss-of-exclusivity opportunity for the off-patent industry, with the first adalimumab rival expected to hit the US market at the end of this month. But with a host of other biosimilars expected to launch throughout the year, how will competition play out in the long term?

With long-awaited biosimilar competition to AbbVie's top-selling Humira (adalimumab) brand finally expected to hit the US in 2023, the off-patent industry is bracing for its biggest ever loss-of-exclusivity opportunity.

While the originator has not yet reported full-year sales figures for 2022, in 2021 US Humira revenues grew by 7.6% to $17.3bn – representing a significant chunk of the brand's global $20.7bn total – with the arthritis treatment only losing its crown as the world's top-selling drug in 2021 when it was unseated by Pfizer/BioNTech's Comirnaty mRNA vaccine for COVID-19. (Also see "*How Humira Finally Lost The Top Spot In Drug Sales*" - Scrip, 29 Dec, 2021.)

However, with multiple biosimilar sponsors already holding US Food and Drug Administration approvals for Humira rivals and awaiting launches throughout the year – along with anticipated competition from further biosimilars that are still awaiting FDA approval – it remains to be seen how competition will shake out among adalimumab rivals.

Complicating the picture are a number of different variables that could influence uptake for individual biosimilar products. As well as launch timing – dictated by a series of settlements

between biosimilars sponsors and originator AbbVie that offer a variety of launch dates throughout 2023 – and price, these factors also include FDA designations of interchangeability for certain products, different concentrations of adalimumab (50mg/ml and 100mg/ml), as well as other attributes such as citrate-free and latex-free presentations.

Amgen Leads The Pack With Late-January Launch

Leading off biosimilar competition to Humira is expected to be Amgen, which saw its Amjevita (adalimumab-atto) 50mg/ml biosimilar approved by the FDA in 2016 and which has the right to launch from 31 January under a global settlement agreement signed with AbbVie in September 2017.

Amgen is expected to have almost six months with the market to itself until a chasing pack of adalimumab biosimilars launch around 1 July.

These include Organon, with its Samsung Bioepis-developed Hadlima (adalimumab-bwwd) version that is expected to be available in both 50mg/ml and 100mg/ml strengths following a recent landmark approval (Also see "*Samsung Bioepis And Organon Get First High-Concentration Adalimumab Nod In US*" - Generics Bulletin, 17 Aug, 2022.); as well as Coherus, with its Yusimry (adalimumab-aqvh) 50mg/ml biosimilar and Boehringer Ingelheim with Cyltezo (adalimumab-adbm) 50mg/ml version.

Fresenius Kabi is also due to launch in July with its Idacio (adalimumab-aacf) lower-concentration version, having received FDA approval towards the end of 2022. (Also see "*Another US Humira Biosimilar Approved As Formularies Offer Access*" - Generics Bulletin, 14 Dec, 2022.)

Standing out as unique among this second wave of approved adalimumab biosimilars is Cyltezo, which was the first rival to Humira to be granted an interchangeability designation by the FDA. (Also see "*First Interchangeable Humira Biosimilar Approved In US*" - Generics Bulletin, 18 Oct, 2021.) This means that it will be eligible for pharmacy-level substitution as permitted by US state law, as well as benefiting from 12 months of first interchangeable biosimilar exclusivity, thus preventing any other 50mg/ml versions from being designated as interchangeable for a year.

Biocon is set to follow this chasing pack of biosimilars with its formerly Viatris-partnered Hulio (adalimumab-fkjp) 50mg/ml version on 31 July, with further 50mg/ml biosimilars set to follow in the form of Sandoz's Hyrimoz (adalimumab-adaz) on 30 September and Pfizer's Abrilada (adalimumab-afzb) on 20 November.

However, these eight FDA-approved adalimumab biosimilars are far from being the only Humira competition on the horizon.

Alvotech And Celltrion Await Approval For High-Concentration Versions

Several major sponsors aiming to play a significant role in the US biosimilar adalimumab market have not yet seen their Humira rivals approved by the FDA.

Alvotech is still expecting its AVT02 candidate – due to be marketed in the US by partner Teva – to be approved as an interchangeable 100mg/ml adalimumab biosimilar, providing it can pass a pending FDA facility inspection. (Also see "*FDA Promises Interchangeability For Alvotech's 100mg/ml Humira Rival – If It Passes Inspection*" - Generics Bulletin, 22 Dec, 2022.)

A settlement with AbbVie offers Alvotech the potential to launch on 1 July, the same day as Boehringer Ingelheim's interchangeable lower-strength Cyltezo. (Also see "*Alvotech Humira Settlement Sets Up Interchangeable Adalimumab Showdown*" - Generics Bulletin, 9 Mar, 2022.)

The hold-up to Alvotech's US FDA nod comes despite approvals and launches for AVT02 in other territories such as Canada and Europe. (Also see "*Alvotech Bullish As Facility Deficiencies Hold Up Humira Biosimilar Again*" - Generics Bulletin, 6 Sep, 2022.)

Meanwhile, Korea's Celltrion is eyeing a Q3 launch date for its own 100mg/ml adalimumab biosimilar that is also still awaiting FDA approval. (Also see "*Settlement Gives Celltrion Date For US Higher-Strength Humira Biosimilar*" - Generics Bulletin, 27 Apr, 2022.)

And further biosimilar variants could be in the works from some of the existing players, with firms such as Sandoz planning 100mg/ml higher-strength versions of already-approved 50mg/ml biosimilars (Also see "*Sandoz's High-Concentration Humira Biosimilar Lands On FDA's Desk*" - Generics Bulletin, 21 Jul, 2022.), as well as players such as Pfizer looking to eventually secure interchangeability designations once any exclusivity periods awarded to rivals expire. (Also see "*FDA To Review Pfizer's Abrilada For Humira Interchangeability*" - Generics Bulletin, 3 Mar, 2022.)

Price, Interchangeability And Concentration

Unsurprisingly given the varying attributes of their adalimumab biosimilars, these competing US players have aired different views on which elements will be crucial to success in such a competitive landscape.

Alvotech has suggested that its anticipated combination of a 100mg/ml higher-strength version with an interchangeability designation will give it the edge in the US market.

With the firm pointing to the higher concentration version of the Humira original now accounting for around 85% of brand use in the US, the company has said that, especially given the likely presence of multiple high-concentration biosimilars in the market, "there will be no big need for the market to convert from the high-concentration back to the older product, which was a worse product." (Also see "*Alvotech Could Upend Expectations For US Humira Biosimilars*" - Generics Bulletin, 3 Feb, 2022.)

And Boehringer Ingelheim has indicated that "the interchangeability status of Cyltezo reinforces our goal of expanding overall treatment options and contributing to the quality and sustainability of the US healthcare system."

However, Amgen – which will enjoy a significant competitive advantage as a result of its early launch date – has suggested that interchangeability is a "nice to have, not a need to have" attribute. (Also see "*Amgen: Humira Interchangeability 'A Nice To Have, Not A Need To Have'*" - Generics Bulletin, 17 Feb, 2022.)

Similarly, Coherus has suggested that the significance of interchangeability could be overplayed, with the firm instead viewing "significant supply capability with low pricing [as] the primary driver of conversion." (Also see "*Coherus: Interchangeability 'A Melting Ice Cube,' Price And Supply Key*" - Generics Bulletin, 21 Mar, 2022.)

Alluding to a competitive pricing strategy, Coherus has promised that its 50mg/ml Yusimry version will be accompanied by a "compelling value proposition" that it hopes will help it to capture market share. (Also see "*Coherus Promises 'Compelling Value Proposition' After US Adalimumab Approval*" - Generics Bulletin, 20 Dec, 2021.)

Towards the end of 2022, further sponsors have also begun jostling for position. Biocon recently said it believed it was "in a very good position as we meet with our payer customers," citing "a lot of European history within our product ... which is key to payers." (Also see "*Biocon Claims Edge For Adalimumab In US*" - Generics Bulletin, 22 Nov, 2022.)

And Organon cited multiple elements as being key to its success with Hadlima, including having both a a high-concentration citrate-free formulation and a low-concentration formulation; real-world evidence from launches in Europe, Canada and Australia; and a pen design that it believes can "deliver a frictionless experience for patients transitioning from Humira." (Also see "*Organon Believes It Can Beat Out Other Humira Rivals In US*" - Generics Bulletin, 16 Nov, 2022.)

Formularies Outline Expectations For Access

As the arrival of Humira biosimilars draws closer, sponsors are also beginning to get a clearer idea of how formularies will approach the unprecedented arrival of so many versions of the same biologic molecule in such a short timeframe.

United Health Group's in-house pharmacy benefit manager Optum Rx recently 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, 2 Dec, 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 has also announced that in 2023 it will "begin recommending Humira biosimilars to sit alongside Humira in the inflammatory drug class on its preferred list of drugs."

For its part, originator AbbVie has predicted "strong access" to Humira in 2023, but said it would not provide sales guidance for the brand until its fourth-quarter earnings call.

AbbVie: Competitor Pricing, Humira Formulary Placement Will Dictate US Biosimilars Impact

By Joseph Haas

02 Nov 2022

Now just months away from the first US Humira biosimilar launch, analysts are asking AbbVie for specifics on expected revenue erosion. CEO Gonzalez said AbbVie aims for 90% formulary coverage in 2023.

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"With regards to the status of contracting for Humira, our intent has always been to maintain broad formulary access so that we can compete effectively with forthcoming biosimilars," said CEO Rick Gonzalez (*see sidebar*).

"We are making very good progress consistent with this objective and are currently projecting formulary access for at least 80% of all US covered lives. We expect this percentage to increase further as we conclude additional contract discussions."

Vizient Survey Ranks Key Adalimumab Attributes

Offering a separate perspective is healthcare organization improvement firm Vizient, which recently published a report – based on a survey to pharmacy executives and professionals – aimed at assessing "factors likely to guide the utilization of Humira competition products, once available." (Also see "*What Aspects Will Give Humira Biosimilars The Edge In 2023?*" - Generics Bulletin, 29 Sep, 2022.)

The report's findings on the top attributes for selecting a preferred biosimilar adalimumab rank payer placement, acquisition price and interchangeability above aspects such as the ease of use of autoinjectors, the absence of citric acid, a higher-concentration product, or patient support programs, although some difference was seen between Community Hospitals Association and non-CHA responses.

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Steven Lucio – Vizient's senior principal of pharmacy solutions – told *Generics Bulletin* that "what we've been encouraging people to do is to go ahead and have early conversations about Humira biosimilars, now, while we're still waiting for their launch," to see "how you could engage with them to find common value and benefit from both the provider and payer perspective."

Referring to the survey's findings, Lucio said "I think this gives us a good insight as to what our audience is thinking at this point – I think it's consistent with what we've been describing [in terms of] the push and pull between the payer and the provider." Key aspects for Humira biosimilars would include "definitely the payer placement and the acquisition price," he confirmed.

Commenting further on the findings, he noted that "given how much conversation there has been about citric acid and the strength – the high concentration – I was maybe expecting that to be a little bit higher."

"The thing that surprised me," he added, "was interchangeability being as prominent as it was, because we've worked very hard to help people not misunderstand interchangeability," which in the US is a legal but not clinical distinction. (Also see "*Cutting Through The Confusion On US Biosimilar Interchangeability*" - Generics Bulletin, 5 Aug, 2022.)

European Experience Points To Heavy Competitive Pressures

While the launch of Humira biosimilars is set to be a watershed moment for the US, the European experience of multiple simultaneous adalimumab biosimilar launches could provide a cautionary tale.

When four biosimilars hit the European market at the same time in late 2018 (Also see "*Four adalimumabs compete in EU*" - Generics Bulletin, 26 Oct, 2018.), heavy price competition resulted almost immediately, with steep discounts reported as competitors battled for market share. (Also see "*UK expects to save 75% from adalimumab rivals*" - Generics Bulletin, 30 Nov, 2018.)

The European market for adalimumab quickly became so competitive that even certain sponsors with approved Humira biosimilars chose not to launch altogether, due to such "unfavorable market conditions." (Also see "*Pfizer Will Not Launch EU Adalimumab*" - Generics Bulletin, 29 Jan, 2020.)

However, it remains to be seen whether the specificities of the US market and the very different aspects at play for next year's cascade of US adalimumab launches result in similarly fierce price competition.

And 2023 signals the starting pistol for adalimumab biosimilars in the US, the Vizient report

suggested that the true impact of Humira biosimilars in this market would only really begin to be seen from 2024.

Given that only one biosimilar, Amjevita, would be on the market from the end of January, with others following only from mid-year, Lucio observed that in terms of formulary decisions, "payers usually make their determination well in advance of the next year. So at what time those molecules could get to the respective formularies is unknown."

"So 2024 is very much where we should be really thinking about."

And AmerisourceBergen's senior director of biosimilar commercialization, Brian Biehn, concurred, recently telling *Generics Bulletin* that "we expect more widespread adoption to occur in 2024…partially because the majority of approved biosimilar products are set to launch in mid-2023" (*see sidebar*).

Humira LOE Is 'Uncharted Territory' As Fierce Competition Expected

By David Wallace

02 Dec 2022

Discussing the latest developments in the US biosimilars market, AmerisourceBergen's senior director of biosimilar commercialization, Brian Biehn, talks about what we can expect from competition to Humira in 2023, how the first ophthalmology biosimilars are faring, and potential changes on the horizon at the FDA that could smooth the path to market for biosimilars sponsors.

Read the full article here

But while he acknowledged the unprecedented competitive landscape that would result from the "uncharted territory" represented by so many adalimumab biosimilars launching in 2023, Biehn nevertheless said it was "important to consider the size of the market."

"Humira is the world's top-selling pharmaceutical product," he underlined. "While developers will compete to gain formulary placement and market share, I believe the market is large enough to sustain multiple players."