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Humira One Year Out: The Largest LOE Event In US Pharma History

Amgen's Amjevita Biosimilar Set To Launch On 31 January 2023 With Many More To Follow

by Dean Rudge

Ahead of the first biosimilar Humira product set to launch in 365 days, *Generics Bulletin* provides a comprehensive run-down of where biosimilar sponsors stand and the key issues ahead of market formation.

Not that it needed spelling out, but Organon's CEO Kevin Ali wished to make sure there were no uncertainties.

"That's going to be the largest loss of exclusivity event in the history of the pharma market in the US," he told attendees to the annual J.P. Morgan Healthcare Conference earlier this month.

The arrival of the first biosimilar to AbbVie's Humira (adalimumab) in exactly one year's time is to mark a watershed moment for industry, as the anti-tumor necrosis factor giant – the flagbearer in the treatment of inflammatory diseases like rheumatoid arthritis and Crohn's disease – finally loses patent protection.

By the close of 2023, it's anticipated that up to seven biosimilar sponsors will have followed Amgen's (likely) lead.

The California-based biotech is set to pioneer competition with its Amjevita (adalimumab-atto) biosimilar, which has the right to launch on 31 January 2023 under a global settlement agreement signed with AbbVie in September 2017.

Amgen is anticipated to enjoy at least a five-month monopoly, before other biosimilar sponsors

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launch their products.

Organon/Samsung Bioepis, Boehringer Ingelheim, Viatris, Sandoz, Fresenius Kabi, Pfizer, and Coherus BioSciences are all set to follow suit later in 2023, also under their own respective licensing agreements.

Will Alvotech Launch At Risk?

While the aforementioned biosimilar sponsors are all in receipt of FDA-approved biologics license applications, other firms have an outside chance to crack the market in the same timeframe.

Amid a recent deferral on its application, caused by a COVID-related delay to an inspection of its facilities, Alvotech is something of an unknown quantity.

It so far has eschewed a settlement deal with AbbVie and instead continued to fight its case in various lawsuits. (Also see "*AbbVie Humira Lawsuit Withstands Alvotech Attack*" - Generics Bulletin, 2 Sep, 2021.)

Ramping up speculation, commercialization partner Teva had recently acknowledged that sponsors in it and Alvotech's position would sometimes choose to launch at-risk; something AbbVie has pointed out in the past, as part of its court filings. (Also see "*AbbVie Sues Alvotech Again Alleging At-Risk Adalimumab Launch*" - Generics Bulletin, 11 Jun, 2021.)

Celltrion, meanwhile, has also not settled with AbbVie – although it, too, has not obtained FDA approval for its application either.

AbbVie Outlines Humira Erosion Expectations

Earlier this month, AbbVie had reiterated its continued expectations for the level of Humira erosion in 2023, based on its experience with the biologic going off patent in Europe in 2018.

The US-based originator is sticking with its past guidance of 45% erosion in 2023 with a plus-or-minus 10% margin for error. (Also see "*AbbVie Maintains US Humira Erosion Belief As 2023 Negotiations Near*" - Generics Bulletin, 13 Jan, 2022.)

But it underlined that it would be in a better position to refine its prediction "later this year," when it began negotiations with payers and insurers to obtain formulary access.

AbbVie management had underlined in October last year that the firm was "close enough now to that 2023 timeframe that you would expect us to be starting the work to ensure formulary access on all of our products. Certainly, Humira is one of those for 2023."

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“This is a [Medicare] Part D market, and we expect payers to exert the most significant influence on its evolution,” Coherus BioSciences had forecasted in September last year.

In the same month, Organon management had drawn a distinction between the now-established market for cancer biosimilars and the burgeoning market for biosimilar inflammation treatment options.

“Pharmacy benefit managers have national force, they can make formulary additions and subtractions pretty quickly, they can move swiftly and efficiently,” Organon had commented.

“We think price is going to move pretty quickly down, not necessarily like small molecule erosion, but there are opportunities ahead,” the US-based player added, reasoning that PBMs would prioritize biosimilars “with the least amount of resistance from their prescriber base.”

Boehringer Holds Interchangeable Product...

In short, matching AbbVie’s current offering for Humira will be key, and sponsors are aware of this reality, considering two key differentiating factors as they prepare their launches: an FDA designation of interchangeability; and an FDA approval referencing AbbVie’s newer version of Humira: the citrate-free, higher-concentration formulation, sold since July 2018.

Interchangeability has long been a thorny issue for biosimilar sponsors. Its designation on a biosimilar product means that the biosimilar may be substituted at the pharmacy for the reference product without intervention from the prescriber.

Boehringer Ingelheim, the German giant with almost no other biosimilars presence, last year saw its Cyltezo (adalimumab-adbm) biosimilar approved as the first US interchangeable biosimilar to Humira, and only the second interchangeable biosimilar overall. (Also see "*First Interchangeable Humira Biosimilar Approved In US*" - Generics Bulletin, 18 Oct, 2021.)

The German firm emphasized that the designation also meant that the biosimilar was deemed interchangeable across all approved Humira indications.

While sponsors including Alvotech and Pfizer are also pursuing interchangeability designations, expected market opener Amgen – despite its best efforts – is forecast to miss out on the designation, as Alvotech’s partner Teva has been quick to point out. (Also see "*Teva: Amgen’s Interchangeable Humira Biosimilar Too Late For January 2023*" - Generics Bulletin, 29 Oct, 2021.)

...While Coherus Distances Itself From Designation

Conversely, Coherus BioSciences has on numerous occasions declared itself an opponent of interchangeability.

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With ambitions to capture at least 10% of the adalimumab market, the California-based biotech has underlined repeatedly that its own patient-focused offering and manufacturing scale enable it to compete, and "match what payers are looking for." (Also see "*Coherus Distances Itself From Biosimilar Interchangeability*" - Generics Bulletin, 7 May, 2021.)

"What we'd say is that our payer research indicates that interchangeability will not be a major impediment to biosimilar adoption specifically in the Humira market," Coherus management had underlined last year.

Nevertheless, the issue of interchangeability is unlikely to disappear. Last year, in the wake of Boehringer's approval, Bernstein Research's Ronny Gal pondered whether "if in the long run, interchangeable biosimilars will be the only biosimilars" for monoclonal antibodies. (Also see "*Will All US Biosimilar mAbs Be Interchangeable In The Long Run?*" - Generics Bulletin, 19 Oct, 2021.)

With Gal highlighting how this indicated that the FDA "has now established the requirements for such approvals," other monoclonal antibodies for inflammation have also emerged as targets, including Janssen's Simponi/Simponi Aria (golimumab). (Also see "*Alvotech Differentiation Plans Include Interchangeable Golimumab*" - Generics Bulletin, 9 Dec, 2021.)

'The Biggest Portion Will Continue To Be 100mg'

The second issue for biosimilar sponsors is the Humira formulation itself. So far, only a limited number of developers have pursued Humira biosimilars with a higher-strength 100mg/ml formulation, with most preferring to focus on lower-concentration 50mg/ml versions.

As well as pursuing interchangeability, Alvotech is also chasing an approval for a biosimilar referencing the newer Humira formulation. It last year saw a delay on its application, caused by obstacles preventing facility inspections. (Also see "*Alvotech Suffers Delay On Higher-Strength Adalimumab In US*" - Generics Bulletin, 21 Sep, 2021.)

Nevertheless, Teva had earlier this month said that it remained confident of Alvotech securing FDA approval, while opining that sponsors offering the latest version of the product will get most market share. (Also see "*Teva Confident On US Adalimumab Filing Amid Alvotech Advantages*" - Generics Bulletin, 13 Jan, 2022.)

Alvotech has previously declared itself as the only known company that has both filed for a high-concentration biosimilar version of Humira and successfully conducted a switching study in support of an FDA designation of interchangeability.

At the end of 2020, Alvotech CEO Robert Wessman told *Generics Bulletin* how his firm had "made switch overnight" from development of the 50mg formulation to the 100mg formulation once it

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became clear that AbbVie was shifting its focus to the higher-concentration version. “I believe they have managed to convert over 80% of the market into 100mg,” Wessman noted.

He also observed that in the US it was “highly unlikely or almost impossible to think that there will be any kind of switch between 50mg and 100mg.” (Also see "*Partnerships Provide Global Foundation For Alvotech*" - Generics Bulletin, 15 Dec, 2020.)

“Of course, the 50mg [biosimilars] will get their share,” he acknowledged, “and potentially they can convert back part of the 100mg [market]. But still the biggest portion, in our mind, will continue to be 100mg.”

Prediction: Four To Six Interchangeable Products Coming

Earlier this month, Samsung Bioepis and Organon revealed that they too were developing a biosimilar referencing the higher concentration formulation. (Also see "*Samsung Bioepis Aims To Compete On Higher-Strength Humira In US*" - Generics Bulletin, 5 Jan, 2022.)

“We’re working as well with our partners to bring forward an interchangeability designation as well,” Organon management had revealed earlier this month.

While no biosimilar sponsor currently had plans to enter the market with an interchangeable, high dose, citrate-free formulation, Organon pointed out, “all of us are kind of working to essentially add that, and the stakes are really the citrate-free, high dose and then, of course, an innovative device as well.”

“We suspect the variability of features without a single player offering the full suite of the product may serve to delay adoption, as would the mid-year timing of entry,” Bernstein’s Gal had forecast in a 21 January note.

“However, over the following two years, we would expect between four and six products offering interchangeability to the most recent version of Humira to enter. This will bring the market closer to a generic-like model and drive the conversion to biosimilars to near complete,” Gal projected.

In the Bernstein analyst’s view, “payers are still hesitant, but we expect a more aggressive attitude over time. None of the biosimilars have made concrete price-volume proposals and it seems the payers will be in a position to make their product choice around mid-year – or a bit later.”

‘Biosimilars Will Adopt A Landgrab Attitude’

Kevin Ali, who had noted the significance of Humira biosimilars next year, described the potential for Humira to be a “whole different animal” to other US biosimilar launches before it.

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(Also see "*Organon: Humira A 'Whole Different Animal' To Other US Biosimilars*" - Generics Bulletin, 11 Jan, 2022.)

"I think PBMs are also going to want optionality, they're not stupid in that respect," he told investors earlier this month. "They're going to want two or three products kind of battling it out – or maybe more – and to see where the price could potentially spiral to."

"The early attitude is cautious with most payers considering delaying adoption until mid-2023 or later or having joint offering of Humira and biosimilars early on," Gal wrote.

"AbbVie appears to be smartly adopting an accommodating policy to slow the transition. However, our suspicion is that the biosimilars will adopt a landgrab attitude and push for early adoption by giving deeper discounts. We expect that both share shift and price decline will end up being somewhat higher."

Wholesaler and distributor AmerisourceBergen had told *Generics Bulletin* last year that it anticipated "rapid adoption of the adalimumab biosimilars once they're available – especially since they are likely to be self-administered."

"We're watching 2023 because the biosimilar market will ignite – six or more FDA-approved biosimilars referencing Humira are set to launch," senior director of biosimilars Sean McGowan commented. (Also see "*'Rapid Adoption' Expected For US Humira Biosimilars*" - Generics Bulletin, 1 Dec, 2021.)

Manufacturing Scale And Supply Will Be Crucial

Gal also joined Coherus in emphasizing the importance of manufacturing scale. (Also see "*Coherus Promises 'Compelling Value Proposition' After US Adalimumab Approval*" - Generics Bulletin, 20 Dec, 2021.)

"We believe that supply is really essential in a large-scale market such as Humira," CEO Denny Lanfear had emphasized during a May 2021 conference call.

"We made significant investments both last year and this year…to increase scale and to be a very large-scale producer," Lanfear pointed out. "We intend to be fully ready when that market opens up…and I think that it's very important to have a very, very robust supply for that market."

Echoing this view, Gal wrote that the sheer size of Humira meant that for biosimilar sponsors, "having the manufacturing capacity that can supply the market is not trivial. For the payer, if it cannot receive the drug, it will have to pay more elsewhere," he observed.

"Large companies with in-house manufacturing have a material advantage. Those that have

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already launched in the EU have also proven their manufacturing capacity."

With one year to go, and key issues still outstanding – not least Alvotech facing a decision by October 2022 in its patent litigation showdown with AbbVie – the landscape could yet evolve beyond today's assumptions around competition to Humira, ahead of the debut launch of Amjevita.

Regardless, the seismic impact of the largest loss of exclusivity event in the history of the US pharma market will reverberate through 2023 and beyond, ushering in a new era of much-needed biosimilar competition for anti-TNF biologics.

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