

July 1, 2023 | News

What's Next? Five Things to Look Out for in July

Floodgates Open for US Humira Biosimilars; Key TB Drug Can Move in India

by **Dean Rudge**

Generics Bulletin previews the most notable and anticipated events for July 2023.

Humira Second Wave Arrives

One of the truly seismic events in US biosimilar history, perhaps the most, will come to pass as the clock ticks into July 1 as the second wave of biosimilar Humira (adalimumab) sponsors – as many as eight – become free to launch their products, five months after Amgen debuted competition.

In the wake of Amgen's Amgevita (adalimumab-atto) – which hit the market in January – Biocon/Fujifilm Kyowa Kirin Biologics' Hulio (adalimumab-fkjp), Boehringer Ingelheim's Cyltezo (adalimumab-adbm), Celltrion's Yuflyma (adalimumab-aaty), Coherus's Yusimry (adalimumab-aqvh) and Fresenius Kabi's Idacio (adalimumab-aacf) will be free to launch, per earlier patent-litigation settlement deals penned between themselves and originator AbbVie.

They can be joined, meanwhile, by Pfizer's Abrilada (adalimumab-afzb), Samsung Bioepis/Organon's Hadlima, (adalimumab-bwwd) and Sandoz's Hyrimoz (adalimumab-adaz), which also brokered agreements allowing for launch.

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.

With so many variables and moving parts to condense, *Generics Bulletin* recently provided an explainer for potential market dynamics, covering issues including strengths and formulations, interchangeability and listing on pharmacy benefit manager formularies. (Also see "[Generics Bulletin Explains: The Next Wave Of US Humira Biosimilars](#)" - *Generics Bulletin*, June 23, 2023.)

Shortly after publication, a major development emerged with news that UnitedHealth Group's major in-house pharmacy benefit manager Optum Rx is to reserve a space at parity to Humira for Cyltezo 50mg/ml, the first and only interchangeable biosimilar to Humira; as well as Hyrimoz, which the US Food and Drug Administration in March approved as citrate-free, high-concentration 100mg/ml formulation. (Also see "[Sandoz, Boehringer's Interchangeable US Humira Biosimilars Land Preferred Status](#)" - *Generics Bulletin*, June 26, 2023.)

Failing to make the grade, however, is Alvotech/Teva's proposed AVT02 rival to Humira, which on June 28 received yet another complete response letter denying approval from the FDA. The CRL noted certain deficiencies which were conveyed following the FDA's reinspection of the company's Reykjavik facility that concluded in March 2023. (Also see "[Alvotech And Teva To Miss US Adalimumab Launch After Further FDA Setback](#)" - *Generics Bulletin*, June 29, 2023.)

Xyrem Authorized Generics Rival Hikma

This month brings an end to Hikma's six-month monopoly on generic competition to Jazz Pharmaceuticals' Xyrem (sodium oxybate) 0.5g/ml oral solution in the US – albeit an eventual authorized generic that was delayed well beyond a planned launch date of mid-2022. (Also see "[Hikma Delivers On Authorized Xyrem In US](#)" - *Generics Bulletin*, Jan. 3, 2023.)

Amneal, Lupin and Endo's Par will be free beginning on 1 July to introduce their own limited volumes of authorized generic versions of the sleep disorder brand, which had sales of around \$1bn last year; a couple of hundred million dollars less than 2021, following the rise of Jazz's Xywav (calcium/ magnesium/potassium/sodium oxybates) follow-on brand.

Hikma, which is the only AG with no limit on volume, has expressed its happiness with its launch, noting that "we are pleased with its performance year to date, which is in line with our expectations."

"We also granted each of Amneal, Lupin and Par a license to launch its own generic high-sodium oxybate product under its abbreviated new drug application on or after Dec. 31, 2025, or earlier under certain circumstances, including the circumstance where Hikma elects to launch its own generic product," Jazz notes.

Bank of America's Jason Gerberry noted recently that although the three additional Xyrem AGs are scheduled to launch, "allocations are fixed based on 2022 Xyrem volumes and on aggregate won't exceed 6% of combined oxybate."

Early last month, Avadel Pharmaceuticals announced the launch in the US of its Lumryz (sodium oxybate) extended-release oral suspension, a 505(b)(2) hybrid product containing the same reference product as Xyrem. (Also see "[Jazz Disputes FDA's Approval Of Lumryz Over Xywav's Orphan Exclusivity, Citing Lack Of Comparative Study](#)" - Pink Sheet, June 24, 2023.)

Rovi Awaits Risperidone Date

Laboratorios Farmacéuticos Rovi's Risvan (risperidone) once-monthly injectable, a proposed 505(b)(2) hybrid version of Janssen-Cilag's Risperdal tablets, will meet its FDA user fee goal date this month.

Earlier this year, the Spanish player submitted final responses to a second complete response letter denying its approval, allowing the FDA to issue the firm with a new user fee goal date of 27 July 2023.

Risvan has been pending FDA approval for more than two years, following Rovi's submission of a new drug application in November 2020. The FDA first informed Rovi of a delay in deciding to grant a marketing authorization, before issuing an initial CRL in September 2021. A second followed in January last year.

Jefferies has described 2023 as a "transitional year" for Rovi, "coming off strong comparisons for its CMO business for Moderna's COVID-19 vaccine and as Rovi invests in future capacity to support further growth."

"Meanwhile," it adds, "the upcoming Risvan PDUFA date on July 27 is a key catalyst, where we expect a partner to be announced post approval."

Rovi earlier this year confirmed that Teva was not in consideration to be its US marketing partner, after the Israeli firm's subsidiary in Spain earlier launched another of Rovi's long-acting injectable treatments for schizophrenia, its Baceq (paliperidone) generic version of Janssen's Xeplion, under a 10-year promotion and distribution agreement.

The Israeli firm has an alliance already in the US with France's MedinCell covering both proposed 505(b)(2) long-acting injectable risperidone and olanzapine products. (Also see "[Teva Prepares To Launch LAI Risperidone After US Approval](#)" - Generics Bulletin, May 2, 2023.)

"Teva is not one of the partners of choice that we're currently having conversations regarding Risvan in the US," Rovi has indicated. However, the firm continues to be in "advanced conversation with different companies."

Bedaquiline Boost For India TB Patients

Generic versions of Johnson & Johnson's Sirturo (bedaquiline) mainstay treatment for

tuberculosis can begin to flood the Indian market in July, following the expiry of the originator's primary patent relating to fumarate salt of the drug during the month.

Such a move is possible for Indian manufacturers, in the crucial battle to provide broader access to bedaquiline in India, after the country's Patent Office in March this year rejected J&J's bid to extend its monopoly into 2027, by declining to grant it a secondary patent.

"The ruling was a result of a 'pre-grant opposition' filed by two TB survivors – Nandita Venkatesan from India, and Phumeza Tisile from South Africa – who both were forced to endure the older, more toxic, drug-resistant TB treatments that lasted up to two years and caused excruciating side effects: they both lost their hearing from the old treatment," explains international medical humanitarian organization Médecins Sans Frontières.

Bedaquiline has been named previously among the TB drugs included in India's national list of essential medicines (NLEM), for which the primary aim is to promote the rational use of drugs with an eye on cost, safety and efficacy, as well as facilitating optimum use of healthcare resources, though medicines on the list generally also go on to be subject to price caps. (Also see "[Pharma Readies For Price Caps On Glargine, Tenzotropin, Lenalidomide In India](#)" - Pink Sheet, Sept. 20, 2022.)

"This year, hundreds of thousands of people who should survive TB will instead die because they cannot afford or don't have access to the best and newest treatments. The end of the bedaquiline patent would result in many of those lives being saved," wrote author John Green earlier this year for *The Washington Post*.

As well as lauding the Indian patent victory, MSF earlier this year demanded that J&J "publicly commit now to not enforce its secondary patents on bedaquiline in all countries with a high burden of TB, and allow generic manufacturers to supply more affordable, quality-assured generic versions of this lifesaving drug to everyone, everywhere who needs it."

"Access to affordable generic versions of bedaquiline is presently being blocked by J&J's secondary patents in at least 25 of the 43 countries with a high burden of TB or drug-resistant TB (DR-TB). With more effective and patient-friendly treatment regimens available for people with DR-TB, there is a need, now more than ever, to accelerate access to affordable treatment and save more lives," it argues.

Malaria Prevention Reaches Data Expiry Date

July brings the expiry of five-year data exclusivity in the US for 60 Degrees Pharmaceuticals' Arakoda (tafenoquine) malaria prevention drug – a year to the day, on July 20, of the earliest date a generic firm could file an ANDA claiming that its application does not infringe the originator's Orange Book listed patents.

Two US patents shielding Arakoda, 10,342,791 and 10,888,558, are both scheduled to expire in December 2035, according to the FDA's Orange Book.

“As of the date of this prospectus,” 60 Degrees noted last month, “to the best of our knowledge, no such notice [of an ANDA filing] has been received by us.”

An FDA advisory committee endorsed the efficacy and safety of Arakoda (tafenoquine) for malaria prevention in adults five years ago, but noted at the time that it was counting on post-marketing studies to provide clarity on questions left unanswered by the “patchwork” of small trials supporting the application. (Also see "[60 Degrees' Arakoda Gets US FDA Panel Nod For Malaria Prophylaxis](#)" - Pink Sheet, July 26, 2018.)

Last year, positive Phase II study data suggesting that Arakoda revealed a positive therapeutic signal in mild-to-moderate COVID-19 disease was published in *New Microbes and New Infections*, a peer-reviewed, open-access journal.