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Sandoz Sees Revolution In US Biosimilars Market

After A Slow Start, Five Years On The US Is Delivering On Its Potential

by David Wallace

Five years on from the first US biosimilar approval, the country's biosimilars market is starting to fulfil its potential, in part driven by a recent oncology "revolution" according to Sandoz' Sheila Frame.

Five years after the US Food and Drug Administration approved the country's first biosimilar – *Sandoz*' Zarxio (filgrastim-sndz) – the US biosimilars market is growing into its potential, according to Sheila Frame of Sandoz.

Speaking exclusively to *Generics Bulletin*, the Sandoz US vice-president for marketing, market access and patient services shared her thoughts on the journey taken by the US biosimilars market over the past five years, as well as the key developments on the horizon for US biosimilars, and what the country could learn from experiences in other jurisdictions.

With Sandoz having recently marked the fifth anniversary of launching the first ever biosimilar approved under the Biologics Price Competition and Innovation Act of 2009 (Also see "*Sandoz' Saynor Insists US Biosimilars Market Is Stepping Up*" - Generics Bulletin, 7 Sep, 2020.), Frame emphasized the company's belief that biosimilars remained a "key contributor to a solution to address healthcare costs overall, and give more patients access to these safe and effective medicines, which I think would certainly alleviate not only the financial pressures but also the access pressures that some patients in the US feel."

Filgrastim Rivals Take Over 80% As 'Revolution' Seen In Oncology

Asked whether the US market was delivering on its potential, five years after the Zarxio approval, Frame said "I think in many ways it is. It's probably a lot slower than what we thought it was

going to be when we first launched five years ago, but if you step back and look at the actual facts in the filgrastim market specifically, the latest IQVIA data from the second quarter of 2020 showed us at just a little over 50% market share."

Meanwhile, one of the earlier rivals to Amgen's Neupogen, Teva's Granix (tbo-filgrastim) – not approved under the BPCIA pathway – was "probably sitting at around 28%-29% market share," Frame added, "so you have around 80% penetration. And then you have Pfizer in there as well."

"I think you have to ask whether 86% penetration in the marketplace at five years is something that you might expect. And in fact it is pretty consistent with what the experience has been in other countries, particularly in Europe which is roughly ten years ahead of us."

"So in that case you could say this is pretty good penetration," Frame commented, even though "it took a while."

However, not all biosimilars in the US had enjoyed similar success, she acknowledged. "I think the contrast in the US that has given a lot of companies pause is really in the case of infliximab, where I don't think they've even hit 10% penetration on biosimilars yet with three in the marketplace."

Nevertheless, recent indicators were more hopeful, Frame suggested. "This year, when you look at what I think is almost a revolution in oncology, with what's been happening with rituximab and bevacizumab, you're seeing really the fastest uptake we've ever seen." (Also see "*US Biosimilars Market Will Benefit From Surge In Launches*" - Generics Bulletin, 22 Apr, 2020.)

"So it looks like oncology is definitely setting the pace and is being much more open to biosimilars," she observed, adding that "I think rheumatology is the big unknown right now."

Interchangeability An 'Unnecessary Hurdle'

Asked about the main factors influencing this differing uptake in various treatment areas, Frame said "I think there's a couple of key factors."

"I think the first one is confidence among prescribers," she said. "So we have seen some misinformation out there, some suspicion on the part of prescribers as to whether they really buy into the concept of biosimilarity."

"I also think the US has put in place a higher hurdle than other countries with the whole notion of interchangeability," Frame suggested. "I think that remains an unnecessary hurdle, at least based on what the experience has been around the world with that."

"In our case, with etanercept for example, we ran a

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number of head-to-head switching trials, then the [interchangeability] rules came out after we had run a couple of Phase III trials in that regard. And we were not going to make the hurdle the regulators had put in place, but had actually done all the work."

"A lot of it comes back to education – do the physicians really understand biosimilarity? – so we have done a lot as an industry I think to try and educate on what that is," Frame said. "And so has the FDA, they have certainly supported that."

The US biosimilar market also suffered from incentive mechanisms that did not always work well together, she suggested. "I think we have got incentives that are sometimes playing against each other, the financial incentives in the system. Rebates on the payer side certainly seems to have been one of the barriers in immunology."

"And then you've got some incentives around pass-through type situations on oncology that have actually helped biosimilars quite a bit, for the first three years when you get a pass-through and then the originator is disadvantaged financially," due to differing reimbursement levels for the biosimilars compared to the older brands.

"So I think you've got some pros, some cons," she summarized.

Learning From Gain-Sharing Initiatives In Europe

"As an industry we've been pushing very much to adopt some of the incentives that have worked in the European systems, for example shared savings models where the system can actually reinvest the savings in better patient care," Frame noted.

"We've advocated for an average sales price plus a higher percentage in the [Medicare] Part B space for physicians, to actually incentivize them financially to use a biosimilar and more quickly adopt it; and I think we probably would advocate something similar in the Part D space as we look to pharmacy benefits when the immunology space opens up."

Asked whether Europe was an applicable model for the US, given the various differences across the healthcare landscape in these different markets, Frame was affirmative. "For sure. They've tried different things that I think the US could maybe leapfrog from."

"Just before COVID there was a biosimilar congress in San Diego and I was on a panel with one of

the payers from the UK and one of the payers from Denmark, and it was interesting because their position was really focused on making sure that the biosimilar marketplace is sustainable – and by that I mean that payers should not be picking one winner."

"And that's a really interesting lesson because if you pick a single biosimilar then the other players end up not having a sustainable business model and flee the market."

"I think there's things like that that would be helpful for the US to maybe really examine and learn from. The shared saving model came from the UK and when you start to see the benefits from that, when it frees up capacity in the system, it really makes a difference."

"So I think we can learn for sure from some of those models, as well as from some of the things that didn't work."

> *"We're trying to take the best of the generics industry and mix it with the best of the branded industry, to come up with a model that provides broader access to more patients at an affordable cost"*

Asked whether the biosimilars industry in general was currently behaving more like a generics model or a specialty model, Frame said "I think right now it's kind of its own dynamic. I think what you're seeing now is this blend of Big Pharma – obviously with Pfizer and Amgen deeply embedded in the marketplace they're playing like Big Pharma – and then you've got Mylan, Teva, Celltrion and others, Coherus, and ourselves, more with generic experience."

"With the people who have been in generics a long time, they say this feels like the small-molecule generic evolution of 15 years ago. But it's definitely really going to be its own thing in the sense that we're trying to take the best of the generics industry and mix it with the best of the branded industry to come up with a model that provides broader access to more patients at an affordable cost – and that's the piece for me that's exciting about what we do."

While the higher development costs for biosimilars made the pricing dynamic "different for sure," Frame suggested that "at the same time, we have lots of cost pressures that everyone is trying to apply to new technology as quickly as we can in order to drive the cost down overall. But it's definitely a significantly bigger investment than you'd need for small molecules."

COVID-19 Creates Opportunities But Shrinks Market

Talking of pressures, Frame observed that the COVID-19 pandemic had brought with it both tailwinds and headwinds for US biosimilars.

On access, she said "I definitely think that there's an opportunity to accelerate it, because the pressures will be different. We have so many people in the context of the economic pressures in the US moving to Medicaid – either they lose their jobs and have to move to Medicaid, or they're on COBRA [Consolidated Omnibus Budget Reconciliation Act continuation insurance] and have to pay quite a bit out of pocket."

"So I definitely thinks it creates an opportunity, and maybe more of a sense of urgency to take a serious look at what the incentives could be, and how they could be set up in order to accelerate the uptake."

But "at the same time, COVID has created a situation where at least in oncology it would seem that patients are staying away from physicians' offices and I think that certainly new patient diagnosis is really down," she pointed out. "And that's even more scary for the system's sustainability overall. Because the later someone is diagnosed, the more difficult they are to treat, and the healthcare outcomes are obviously much less beneficial to the patient."

"So I think that's the piece that we just don't know yet, as we're into month seven of this situation in the US. If people are staying away from treatment and diagnosis then that shrinks your market at the same time. So I think it's a little bit of a difficult one."

Still Opportunities To Achieve Greater Savings

Turning to the savings potential of biosimilars – with biosimilar filgrastim alone having generated savings of more than $1bn – Frame pointed to opportunities to increase the savings from biosimilars even further in the US.

"I think it comes back to the system," she said. "I think in the context of the system in the US, [biosimilars] have been incredibly successful." But "I think it all comes down to the way that the system is currently set up."

The US system "favors the incumbent," she noted, "so the biggest market share if you're in a rebate system makes it very hard – if you don't have that forced conversion that you've seen in more socialized medicines systems – if you don't have that forced conversion quickly, then it's not economically feasible for someone to favor your biosimilar over the originator."

Pointing to possible legislative solutions, she said "we'll have to see whether or not some of the discussions – I think there are five bills at the moment that include a biosimilar provision, whether it's shared savings or additional incentives – whether or not they can accelerate through Congress in order to open that up."

On filgrastim specifically, she highlighted that "filgrastim came into the marketplace largely aligned with new patient diagnosis and new cycles. People weren't necessarily converting existing patients in the middle of a cycle of treatment. And of course filgrastim and pegfilgrastim both are relatively short-term treatments. It's not like what you're seeing with rituximab, bevacizumab or trastuzumab."

"And so I think the biggest opportunity that I would say is lost savings – and certainly we've seen that in the infliximab case – [is that] there is tremendous opportunity for additional savings there if there was a way to more quickly transition patients off the originator to the biosimilar. And that's certainly what we've seen in other countries where, when the biosimilar is favored – except in cases of medical necessity – you'll see the savings very quickly."

"At the same time," she said, "I think it's really important to look to the future. We have a number of biologics coming off-patent in the next five to 10 years, and I think that's where we're going to see the US market really open up."

> ***"We're continuing to challenge the etanercept patent situation. And if we are not able to overcome that, then etanercept will have been in the marketplace for 30 years. There's not a patent system in the world that ever contemplated that kind of monopoly."***

Asked whether US intellectual-property protections for biologic brands were still a big part of the problem for biosimilars – with the industry in the past having pointed to "patent thickets" that were unfairly shielding major biologics from competition (Also see "*AAM Urges Action On Product Hopping And Patent Thickets*" - Generics Bulletin, 26 Sep, 2019.) – Frame said that "for sure the US system for IP is quite different to the rest of the world. At Sandoz we've continued to be the major pioneer – *we went all the way to the Supreme Court and won* – and so we've started to chip away at what you might perceive as a barrier."

"But certainly to try and open up the system more quickly we're continuing to challenge on the etanercept patent situation," Frame noted, referring to the ongoing litigation over Enbrel. (Also see "*Sandoz Seeks Review Of Enbrel Ruling*" - Generics Bulletin, 4 Aug, 2020.) "And if we are not able to overcome that, then etanercept will have been in the marketplace for 30 years. Now there's not a patent system in the world that ever contemplated that kind of monopoly domination."

“So I think we’re going to keep trying to open the system up,” Frame said.

“Now at the same time, I think we all feel pretty strongly that patents are a fundamental need for innovation. Patents were founded as a way to protect the inventor but also enable follow-on innovation. But there is a point at which the marketplace needs to really open up.”

“And so that’s why we feel in the US that we’ll keep challenging where we can, and where there is a real need to bring our products to the market in a reasonable time.”

FDA And Canadian Campaigns Bolster Awareness

Turning to public campaigns to drive awareness on biosimilars – including from the FDA in the US – Frame said Sandoz was “certainly thrilled with the FDA campaign.”

“I think that, as a partner in that, on behalf of the industry, I think the credibility and leadership that the FDA has been able to demonstrate with respect to increasing education overall is very helpful. I do think that generally people have greater faith in information and education that they’re going to get from either the regulatory agencies or from government officials or from their healthcare providers. So I think that all of those kinds of things are super helpful.”

“We certainly work with a lot of the patient advocacy organizations to provide balanced and fair information to reassure the marketplace that the products we’re bringing are safe and effective,” Frame underlined. “So I definitely think that there’s an opportunity to continue to educate in that regard, around the world.”

And in general, she suggested, “I do think that in the US there is much more openness today to the experiences in other countries. We know that [managed care consortium] Kaiser Permanente have looked to the Canadian system, where there has been significant transformation in the province of British Columbia last year.” (Also see "*British Columbia Starts Biosimilar Switching Program*" - Generics Bulletin, 29 May, 2019.)

Through a biosimilar switching program, the Canadian province “actually converted the etanercept marketplace to favor biosimilars, and in doing so were able to demonstrate directly to the public how they reinvested those savings into opening up the formulary there for new innovations,” Frame noted. “And so they took the savings and immediately applied them to funding new products that were coming to treat patients.”

“I think those kinds of examples are certainly much more applicable in the US marketplace today than they might have been.”

Tide Is Turning On Misinformation

Asked whether the tide was turning on misinformation around biosimilars, Frame was emphatic.

“For sure. I worked in immunology for a long time, and I think about the American College of Rheumatology and its evolution over the course of the last, let’s say, three to five years, where rheumatologists were initially saying ‘not on my watch’ to today saying ‘well of course I would prescribe a biosimilar if available’.”

“So I think that confidence in biosimilars and a more deep understanding, I definitely think that that has transformed and we’ll see a lot more of that.”

Meanwhile, FDA efforts to address misinformation also seemed effective, she said. “They’ve invited us repeatedly as an industry to provide the examples of where we’re seeing misinformation, and they’re going after it. And it seems to be being acted on quickly,” she said, acknowledging that “when you bring it forward, they don’t tell you what they do with it, but it would seem that they are taking action.”

Suffix Naming Convention Remains ‘An Irritation’

On the subject of US naming conventions – and whether the FDA’s decision to apply meaningless four-letter suffixes to the non-proprietary names of biosimilars, unlike other major territories, was a hindrance to the US biosimilars market (Also see "*FDA Sticks To Its Guns On Biosimilar Naming*" - Generics Bulletin, 8 Mar, 2019.) – Frame said “I would describe it more as an irritation. I think in the hierarchy of needs of legislative change I’m not sure I’d put it at the top of the list, but I do think it’s a bit of an irritation.”

“It’s a bit like interchangeability: why does the US have to be so different than the rest of the world in this regard, and to what end?”

“I think initially we thought it was fine if every biologic was going to have to have a different suffix, but the fact that the originators now do not seems a little odd,” Frame further observed.

“I don’t know that I would say we have prioritized it as a key hindrance, [but] we’d like to see it not there.”

2020 Is The Year For Oncology; Adalimumab Rivals Hit In 2023

Looking ahead to key developments on the horizon for the US biosimilars industry, Frame gave a positive overview. “We’ve got some data that would say that 1.2 million US patients could gain access to biologics by 2025, just because of the availability of the biologics that are going to biosimilars that will be available by then,” she suggested.

“And in particular, in the US at least, the patients that tend to benefit are lower-income, women and the elderly, so you’re going to be able to provide access and benefits to people that otherwise would not have them. So I think there’s a huge opportunity just with the biosimilars that have been approved already.”

“But I think if you look at the next wave coming, you think about immuno-oncology as the big wave that will come off-patent in the 2026-2030 timeframe, then by then biosimilars will be much like what the generics market is. I think we’ll see a significant portion of the marketplace being treated with biosimilars as they come into the marketplace, so I think that’s pretty exciting.”

And in the nearer-term, Frame said “I think the insulin market in the next two to three years might be very interesting to see what happens. [There is] a lot of legislative focus on that, a lot of patient need in insulin, so we’ll see how that evolves.”

“If I was going to prioritize the marketplace, I think that oncology is going to lead the way in the short and longer term, just because of the way in which those patents are coming off; I think immunology has started, with infliximab, and we’ll see if etanercept actually wins, getting through the legal barriers – and then adalimumab will be a huge boost in 2023 as there are nine or ten all coming to the market at around the same time, so that will be very interesting (Also see "*Biosimilar Humira Settlements Stand Firm In US*" - Generics Bulletin, 10 Jun, 2020.); and then I think insulins in the shorter term; and ophthalmics in the longer term.”

“And then we’ll see what happens as innovation continues. We certainly have a very broad portfolio in biosimilar development looking out towards 2030.”

“When you look at the marketplace and who’s emerging,” Frame concluded, “I think Sandoz will always be committed to – and a leader in – the biosimilars space.” Pointing to changing trends among major players in the market, she said “I think Coherus has indicated that they’re shifting more to a branded space, I think Pfizer has said they’re not going to have their longer-term portfolio, Merck got out of the insulin business.”

“So I think you’re going to see this evolve much more as a generic-type marketplace, and that’s where I think Sandoz is definitely a winner in that regard.”

In part two of this interview, Sheila Frame talks about specific biosimilar opportunities for Sandoz in the US and Canada. (Also see "Sandoz Looks Ahead To Biosimilar Opportunities" - Generics Bulletin, 28 Sep, 2020.)