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Taking European Biosimilars To The Next Level

Industry Experts Talk About How Europe Can Build On Successful Progress Made So Far

by David Wallace

Europe's biosimilars market now has many years of progress under its belt. But how can this successful foundation be built upon to make the most of the opportunities on the horizon and achieve even greater access and uptake? In an exclusive interview, *Generics Bulletin* talks to Medicines for Europe's Isabell Remus and Julie Maréchal-Jamil about the next steps.

Europe represents the world's most mature biosimilars market, with almost 20 years of experience and billions of patient treatment days with biosimilar medicines.

But at Medicines for Europe's 20th annual biosimilar medicines conference, held in Amsterdam in April, attendees were asked to consider what the next 10 years might look like for biosimilars: how to build on the region's successful foundations to deliver greater and faster advances in uptake and access.

Speaking with *Generics Bulletin* on the sidelines of the conference, Isabell Remus, chair of Medicines for Europe's biosimilar medicines sector group and head of biopharma and specialty at Sandoz, and Julie Maréchal-Jamil, director of biosimilar policy and science at Medicines for Europe, discussed the key areas that industry and regulators need to focus on to best take advantage of the opportunities offered by biosimilars.

Asked to summarize the story so far, Remus noted that "it's now 18 years since biosimilars are on the market, and I think there's been a really good evolution."

European Progress On Biosimilars Is

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"If you look at it in terms of number of molecules," she pointed out, Europe had authorized biosimilars for 27 reference medicines, with "over 100 biosimilar applications with positive [European Medicines Agency] opinions."

And "in terms of adoption in the market, we see with every launch goes faster, the savings that were generated, I think there's really a very nice evolution."

"I think we can say that Europe by now is the number one market in terms of biosimilar experience, clinical experience – with 5.8 billion cumulative patient treatment days – and trust that we have from the different stakeholders. So I would say we're still leading the way here in Europe after 18 years and we are very happy about that."

Just The Beginning

By David Wallace

07 May 2024

Speaking at Medicines for Europe's 20th annual biosimilar medicines conference, Isabell Remus, chair of Medicines for Europe's biosimilar medicines sector group, looks to the future for European biosimilars over the next decade and outlines the potential that can be realized – but only if a comprehensive strategy for biosimilars is put in place.

Read the full article here

But with Medicines for Europe urging the European authorities to put in place a more comprehensive strategy for biosimilars (*see sidebar*), Remus was asked whether there were any existing examples of good practice that could be a model for the region.

"First of all, we've got very positive examples when we look at uptake," she said. "So if I look at the Nordics, if I look at Germany, if I look at Italy, large markets – and not just large markets, also smaller markets – the way they implement or leverage the opportunities is very positive."

"If I look at the therapeutic areas, the way oncology is embracing biosimilars now I think is very, very positive. And also if I look at how prescription is picking up, also on the immunology side, now faster and faster adoption, we see it's part of the treatment regime. So I would say there's a lot of positives."

"So now," she suggested, "it's about building on what we know. Of course some markets are more attractive than others when it comes to that. But also we're seeing – if I look at the UK and how they recently differentiated biosimilars from other products, when it comes to the clawback discussion – there's clearly recognition that biosimilars need to be appreciated and treasured and seen as part of the solution." (Also see "*BGMA Warms Up To UK's VPAG Scheme*" - Generics Bulletin, 20 Dec, 2023.)

Markets like France had implemented incentives for uptake, she highlighted. "They've got

targets in terms of biosimilar adoption and they have implemented incentives for accounts departments to actually use that in practice. So I would say also it is a positive."

But "it doesn't mean it's across all of Europe," she acknowledged. "I think we still see further opportunities for improvement on a number of fronts."

While "the question of whether biosimilars have value and can be trusted" was by this point "quite clear," she said, "now it's time to elevate this understanding and implement their usage on a broader scale." This meant that "we need to look at the balance of what's been achieved, and now take those learnings or those results and apply them more broadly."

More Nuanced Conversations With Different Stakeholders

One key aspect highlighted by Maréchal-Jamil was the need to tailor conversations to stakeholders who had differing levels of familiarity with biosimilars.

"We are in a cycle where basically we've had a lot of immunology products, a lot of oncology products. We often have the second, third, or fourth biosimilar medicine available," she observed. "So in that context of familiarity, the incentives are evolving in their nature. It's a different landscape, which we could call it mature."

But at the same time, she pointed out, there were still stakeholders "which have not yet heard of biosimilar medicines or not used biosimilar versions of a medicine." In newer therapeutic areas like ophthalmology or multiple sclerosis, "the question is, are we actually equipped to start the conversation over, where it's at the very early stage? We probably need to start to nuance or tailor interventions and the setup to take account of the level of familiarity with biosimilar medicines."

"Because these are new stakeholders to the table – they are where we were earlier in other therapy areas, and we shouldn't presume or assume that the general biosimilar experience can be directly extrapolated. We should not assume ophthalmologists are directly talking with oncologists about their biosimilar medicines or seeing the relevance of their experience."

This was "something we're discussing with the regulators as well," Maréchal-Jamil said, suggesting that "there remains

Sandoz Rolls Out Natalizumab Biosimilar In Germany

By David Wallace

31 Jan 2024
Sandoz is rolling out its Tyruko natalizumab biosimilar rival to Biogen's Tysabri in Germany, heralding the product as the "first and only biosimilar for multiple sclerosis."

Read the full article here

work to do in information and outreach, in spite of the existing resources. Regulators maybe need to start at the beginning with the newly relevant medical societies."

Remus agreed, but also suggested that "I can see that the process of building trust and gaining expertise became faster. So for example, in Sandoz, we are currently launching into the MS space and we have the first MS biosimilar (*see sidebar*), and I can see that it's an easier discussion. There's more knowledge with different stakeholders. People have heard or used things, or have heard it from other therapeutic areas. So I can see that the barriers can be faster addressed and overcome. And I think that makes me optimistic."

But she underlined that "we should never take awareness or trust for granted – [we need] to make sure we take people on board."

National Scorecards Offer Ideal Policy Comparisons

Asked about specific aspects of national and European-level approaches that would help biosimilars to make further progress, Maréchal-Jamil referred to earlier scorecards for biosimilar sustainability that Medicines for Europe compiled in collaboration with IQVIA some years ago.

These ratings detailed how efficient the policies of 12 European countries were in encouraging healthy competition, comparing various national aspects to an "ideal policy" scorecard (*see sidebar*).

"The idea was not to compare countries to one another, given the many differences in healthcare system set-up and financing, but to allow countries to assess themselves against an ideal," Maréchal-Jamil explained. "We did this work with IQVIA a few years back and I think these elements have not much changed." But "the additional nuance that we can maybe add now is perhaps how the country is using the originator at the time of biosimilar entry," she suggested. "We have observed it is an important nuancing factor that affects how fast the biosimilar framework works."

European Industry Backs Biosimilars 'Scorecards'

By Akriti Seth

14 Jul 2020
Medicines for Europe and IQVIA have partnered to test biosimilar sustainability in 12 European countries by issuing scorecards that measure the contribution of a country's biosimilar policies to health systems.

Read the full article here

There was "also the question of budget constraints, health and pharmaceutical budget constraints, which we didn't have really in the scorecard at the time, but obviously we see impacting uptake and access development in some countries," Maréchal-Jamil acknowledged. "The example of Poland is striking: excellent biosimilar uptake (>80%) in anti-TNF biosimilar

use, yet remains 200-fold less anti-TNF use than the lead country in Europe."

But "overall, the scorecard elements remain the same: clarity of the guidelines, confidence in use, and then all the market mechanics such as pricing, reimbursement, tendering design and incentives."

> *"The next level that I think we need to focus on is the sustainability of the business, of the model."*

For Remus, a key topic was also the overall sustainability of the biosimilars business. "And here, the question is around ensuring that there are multiple players that can have access to the market."

An important factor was "making sure that products are procured not purely based on lowest price but on other criteria as well," she outlined. "You've got markets like Spain that allow for that, where for example, other criteria or services can be built into the offer. You've got markets like France where the price is only 40% to 50% of a tender. There's other criteria of value as well. Or the Nordics that are increasingly adding environmental factors to it. And I think we just learned that they're also looking at multiple winners potentially."

"So that means that yes, there are differences. As Julie said, the scorecard per se sets the framework. The adoption is different. But I think the criteria remain."

"And now the next level that I think we need to focus on is the sustainability of the business, of the model. And here we do see differences in terms of how countries have adopted some really good examples. And now it's about again, taking those and implementing them."

Still Room For Improvement On Access

Asked whether progress was being made on equality of access to biosimilars across Europe – with Medicines for Europe having long highlighted disparities between different countries within the EU (*see sidebar*) – Remus said it was "heartbreaking to see that we still don't have the equal access."

"We have biosimilars on the market now for 18 years in multiple therapeutic areas, and we have a solution, but we don't see that it's being leveraged to its full potential," she lamented.

But "I would say that we are ready to continue to offer that solution. We need governments, we

need payers, prescribers to all now work together on leveraging this opportunity."

"We do know that today that patients with rheumatology or psoriasis conditions can experience significant health improvements by taking biologics or biosimilars. And still, if I look at Poland, only a tenth of what we believe the potential patients are, are having access to therapy."

While "progress is being made with an increase in potential prescribers," she suggested, "it is still concerning that so many patients are not receiving these treatments. It's really mind bogging that it's not happening at the speed that it could and should."

European Industry Urges Action On Unequal Access To Biosimilars

By David Wallace

14 Dec 2023

As the European Commission held an annual event for biosimilars industry stakeholders, Medicines for Europe highlighted continuing inequalities in access across Europe and called for both EU- and national-level action to address this "major concern."

Read the full article here

Maréchal-Jamil said that a big part of the problem was that "countries have been satisfied by measuring a limited number of metrics such as biosimilar uptake and savings. I think that unfortunately this is not the value proposition that we come in with, certainly not in maturing therapy areas where many biosimilar medicines are now available."

"So many countries are satisfied with metrics that are not relevant to actual patient health or outcomes," she pointed out. "It is all good to report 90% biosimilar uptake, but it is equally important to put that in perspective: 90% of what? If the baseline scenario is that the country was treating half or 10% of the eligible population, well, good for those patients, but the waiting list is getting longer and the biosimilar opportunity is largely untapped to resolve this treatment gap."

And even more important than access "as a non-specific term," Maréchal-Jamil argued, was "*timely* access. "Because we know in cancer, we know in chronic diseases, in rheumatology, there are what clinicians call 'windows of opportunity', both from the patient journey perspective, patient outcome perspective, but also for the healthcare system."

"The question of timely access, beyond the sole question of access, is highly relevant to patient pathway improvements and efficiency of healthcare interventions," she emphasized. "It is something that we are also trying to engage stakeholders in. It's no longer about, are you getting it or not, but when are you getting it? Because we cannot be satisfied with getting medicines after a two-year waiting list – because again, we've missed the health objectives."

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Regulatory Streamlining Is Not A 'Silver Bullet'

Remus and Maréchal-Jamil were also asked about opportunities arising from moves to streamline regulatory pathways for biosimilars, with the European Medicines Agency having earlier this year opened up a consultation on whether comparative efficacy studies were always necessary to support biosimilar applications, as part of longer-term moves towards a more streamlined approach (*see sidebar*).

On the question of whether this could open up many more biologic brands to biosimilars competition, Remus acknowledged that "of course if we have a more efficient way to bring these drugs to the market, the threshold will be lowered and that will allow more biosimilars with a smaller originator size, let's say, to be developed. The clinical cost is presumably a key driver of the lack of competition, particularly on smaller molecules."

"Now it doesn't mean the science cannot be robust. I mean, that must always be assured. So that's really important. But of course, streamlining of regulatory requirements does open up the potential for more biosimilars."

EMA Mulls Dropping Comparative Efficacy Trials For Biosimilars

By David Wallace

06 Feb 2024

In a move that could hold major promise for the biosimilars industry, the European Medicines Agency has opened up a consultation on re-evaluating the need for comparative efficacy studies to support biosimilar applications.

Read the full article here

But Maréchal-Jamil suggested that "on its own, streamlining clinical development for biosimilar medicines is not enough, because the challenges around lower number of developments in some areas are multiple."

"The market dynamics are getting more complex. There's technology issues, there's value chain distribution in the system, access issues to special administration centers, etc. And yes, the R&D investments in a biosimilar candidate are a very significant piece of the puzzle, yet not a silver bullet."

And "the other nuancing part I would like to bring forward," Maréchal-Jamil added, "is that Europe needs to move, and it needs to help the rest of the globe move, because companies are developing for Europe and the world. If we had to double or add studies, that would make developments even more complicated – this is certainly not helping, and a unilateral European move will not be sufficient.

Ultimately, she urged, "we need a global regulatory roadmap on biosimilar development

streamlining so that the regulators move. We know regulators need time to adapt guidelines and implement that, but I think Europe moving is really important."

And asked whether removing the need for confirmatory efficacy data would then put even more focus on the analytical stage, Maréchal-Jamil suggested that "the underlying bioanalytical comparability grounds will remain as fundamental for any regulatory-science evolution. The focus has always been there [bioanalytical comparability] and companies and regulators are doubling down on making sure it's ultra robust."

"So I don't think there's any leniency on the program. I think it's quite the opposite. Theoretically, some could consider streamlining clinical development is 'lowering the regulatory bar', the financial bar, when actually the technological requirements and capabilities inherent to the analytical comparability are a rather complex game, far from plug-and-play. And it's worth it, by the look of the vast European experience."

Europe Still Leading The Way On Biosimilars

As Europe navigated these nuances and complexities, the region was nevertheless continuing to lead the way on biosimilars, Remus indicated. This included influencing other leading global regulators, such as the US Food and Drug Administration which is increasingly reconsidering its interchangeability designation that is separate to an agency determination of biosimilarity (*see sidebar*).

"We are happy to see that efforts are being made to align regulatory requirements," Remus commented. "The growing belief in the science behind biosimilars, along with positive market experiences, has contributed to this progress."

"So we are very happy to see the US discuss the interchangeability designation. I think that's a really important way forward. And it actually shows that the FDA is now looking at science, right, and asking themselves if Phase III really needed and that's one way to further drive convergence."

Biosimilar Interchangeability Designation Would Be Nixed Under Biden Proposal

By Derrick Gingery

12 Mar 2024

The proposal is not expected to cost or save the government money, but is expected to increase biosimilar uptake, according to budget documents.

Read the full article here

"So I think that's an absolute positive thing, and I do hope that Europe will lead the way further looking at the next science that's out there, and implementing that."

Looking at the future for European biosimilars more broadly, Remus said "I think number one is really this large opportunity we see with 110 molecules opening up in the next decade. I mean, that's just unprecedented and still we don't see that all of them have development. One in three blockbusters have development ongoing. And that I think is really, really striking."

"So that I think is one of the key developments that we need to see, is how do we actually tap into that opportunity. Then that's why you need the strategy part and the observatory. I think these are the two things that are really key."

"And then last but not least," Remus concluded, "I think it's this whole notion of ensuring sustainability. We must set the right framework for markets across Europe, to ensure that there's a sustainable, attractive model that actually flourishes as we go on."

Industry Needs Answers On New Technologies

Meanwhile, looking towards potential new frontiers in terms of biosimilar development for more complex technologies, Maréchal-Jamil acknowledged that national budget constraints and the "growing weight on pharmaceutical budget for new kinds of biotechnological therapies" would play a key role.

"Before there is any industrial commitment by the off-patent sector, there needs to be a discussion around, what's the vision in Europe for those kind of health technologies," she suggested. "Because one can pull and push, but I think at some point it probably needs a different way of handling everything from development to the access model. And that won't happen overnight."

"So we should start priming that conversation, not knowing where it's going to lead – but the growing weight in budgets cannot be ignored. Sooner or later, it will need an answer, a responsible answer."

"If the answer is, 'well, off-patent-versions cannot be developed', then we can all align and move on. If however the answer is 'we have an ambition to create something here, provide a virtuous cycle involving competition', then we need to be going to the drawing board."