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DRUG BENEFIT NEWS

As Uncertainties About Biosimilars Abound, Payers Cautiously Hail Zarxio Approval

Amid rising drug costs due to a multitude of factors (see story, p. 3), payers this month were given something to cheer about as the first U.S. biosimilar completed the accelerated approval pathway authorized by the Affordable Care Act. But the March 6 approval of Zarxio (filgrastim-sndz) — a copycat version of Amgen Inc.'s Neupogen (filgrastim) for the treatment of infection in certain cancer patients undergoing chemotherapy — was marked by several unknowns, starting with when it will actually hit the market and at what cost.

Beyond that, payers' efforts to accelerate the adoption of Zarxio and other biosimilars in development may be determined by the medical community's willingness to prescribe the new agents, whether biosimilars can share the same nonproprietary names as their reference drugs, and what data the FDA needs to determine that a biosimilar can be deemed interchangeable, industry insiders tell *DBN*.

Zarxio was developed by Sandoz Inc., a Novartis Group company, and received the same five indications as Neupogen. The biosimilar is already being marketed in 40 countries outside the U.S. under the name Zarxio. Neupogen generated $1.4 billion in sales last year, nearly 84% of which were in the U.S., according to Express Scripts Holding Co.

The FDA determined that Zarxio has "no clinically meaningful differences" from the innovator biologic; Sandoz did not apply for status as an interchangeable biosimilar. Sandoz has not disclosed pricing information, although industry expectations are that biosimilars will be available at 30% below the cost of their innovator product.

Payers Prepare for Zarxio Launch

"There are a lot of unknowns as we begin the age of biosimilars, so to speak. I think payers are greatly interested that it be economically viable for the entrants in the market and that there be a long-term commitment to the market," observes Jim Langley, chair of the healthcare and life sciences practice at Mead Consulting Group and a former senior vice president at Accredo Health Group. "There's no doubt that PBMs in particular have some worry that biosimilars simply won't be profitable for enough companies to invest in to develop enough competition for them to have more room to negotiate pricing."

Prime Therapeutics, LLC, for one, remained cautiously optimistic about the approval of Zarxio for reasons outlined in a February report sponsored by Prime and authored by health economist Alex Brill. The report, *The Economic Viability of a U.S. Biosimilars Industry*, proposes that the market for biosimilars may not be as rich as anticipated because of economic and regulatory challenges such as the naming conventions, the clinical testing requirements the FDA may require biosimilars to repeat — which has yet to be finalized by the agency — and state laws that may impact biosimilar substitution. Until such hurdles are resolved, it may only be economically viable for manufacturers to develop biosimilars for blockbuster specialty drugs, suggests the report.

The FDA gave Zarxio the placeholder nonproprietary name "filgrastim-sndz," but said this designation should "not be viewed as reflective of the agency's decision on a comprehensive naming policy for biosimilar and other biological products." While the FDA has not yet posted draft guidance on how current and future biological products marketed in the U.S. should be named, the agency said it intends to do so in the near future.

"How biosimilars are named is critical to their success," argues David Lassen, Pharm.D., chief clinical officer for Prime. He tells *DBN* sister publication *Specialty Pharmacy News* that the Blues plan-owned PBM has "urged the FDA to adopt a naming system where each approved biosimilar is assigned the same nonproprietary name as the approved reference biologic because it will help doctors easily substitute the highly similar, lower cost medicine just as we do for generics now." In Zarxio's case, the "sndz" suffix identifying the manufacturer allows for Zarxio to be grouped with the reference product in compendia, although it is "completely unnecessary given it is accounted for in the [National Drug Code] number," he contends.

"This is the beginning of what we believe will be a wave over the next several years that will help our customers save many, many billions of dollars," remarks Glen Stettin, M.D., senior vice president for clinical, research and new solutions at Express Scripts.

The company estimates that Zarxio has the potential to save U.S. patients and payers $5.7 billion between 2014 and 2024 *(DBN 12/19/14, p. 4)*. That analysis assumes a 30% discount in price for biosimilars and use by 30% of patients new to therapy rather than people switching over from the reference product. Moreover, if the FDA approves biosimilar versions of 11 selected biologics, an estimated $250 billion in savings over the next 10 years could be realized, predicts the PBM.

Meanwhile, three other biosimilar applications have been submitted to the FDA. They are: Celltrion's infliximab (reference drug Remicade), Apotex's filgrastim and pegfilgrastim (reference drug Neulasta), and Hospira's epoetin alfa (reference drugs Epogen and Procrit). Langley estimates that biologics worth at least $90 billion in 2013 global sales will come off patent between 2013 and 2020, and most of them have biosimilars in development (see chart, p. 7).

"The big challenge we foresee is that unlike traditional small molecule generic drugs, we don't expect that these drugs will be able to be substituted without having to go back to the doctor and get a new prescription," Stettin tells *DBN*. If that's the case, Express Scripts will pursue step therapy programs to encourage the use of biosimilars or adopt an exclusionary strategy as it has done with competitors of the hepatitis C drug Viekira Pak and in other classes on its National Preferred Formulary. Moreover, using its Accredo specialty pharmacy to "affect the share and utilization of particular products" is another potential tool for facilitating biosimilar uptake, he suggests.

"Formulary exclusions are absolutely the key strategy here. A brand-to-brand competition model is what we'll see emerge in the biosimilar space, where PBMs will attempt to negotiate with the brand or biosimilar manufacturer, for as deep the rebates as they can get, with the carrot being formulary exclusion for the loser," predicts Langley. "It is not a coincidence if you go back to the plan years of 2013 and 2014 that Express Scripts and CVS Health began…excluding [biologics in certain categories] from their national preferred formularies. I believe they were beginning to set the table for biosimilars."

With traditional generics, if a generic is available and the prescriber hasn't insisted on the brand, the pharmacist is permitted by law to dispense the generic. But eight states have already enacted laws placing various restrictions on when and how pharmacists can substitute biosimilars, points out Phil DeNucci, R.Ph., a managing consultant with The Burchfield Group.

As a result, DeNucci recommends that health plans incorporate design language that will allow the payer to manage biosimilars. For example, they should include a cost share level using the broader term "select alternatives" as opposed to specific words such as "generics" or 'biosimilars." Plans could consider waiving the cost share for members who accept select alternative products, he advises.

In the case of Zarxio, because it is given to patients undergoing chemotherapy, it is typically administered in a physician's office suite and thus billed through the medical benefit. Hence, this and other biosimilars that are physician-administered will require medical benefit management, which can be more difficult for health plans to coordinate and even harder for PBMs to pull off but can be done, says DeNucci. "Medical claims systems can still put in prior authorization or prior approval of products, or they can do a grace fill and say this is the preferred product," he advises.

But if a provider's office or other facility is already making money by dispensing the brand product, plans will have to "look deeper into their contracting where alternatives are becoming available and make sure that their policies support the actual buying scenario" (e.g., establishing fees that encourage the dispensing of the biosimilar product), continues DeNucci. "Those are very specific items that you need to address at a provider contract level. What I think this will hopefully do is deepen the conversation around overall management of high cost products on the medical side."

Christopher Bradbury, vice president, integrated clinical and specialty drug solutions for Cigna Pharmacy Management, says the Cigna Corp. pharmacy unit is "excited" about the approval of Zarxio and has "great confidence" in its efficacy and safety. "We expect biosimilars to create a new level of competition with manufacturers. Increased competition yields better affordability — and we expect that to be the case with Zarxio and Neupogen, especially given available utilization management capabilities and preferred drug strategies," he tells *DBN*. "When launched, the availability of Zarxio (and future biosimilars) will enhance our existing strategies to promote affordability across both medical and pharmacy benefits for Cigna customers and clients."

Catamaran Corp., which has a long-term PBM relationship with Cigna, adds that it plans to manage Zarxio like any drug that comes to market — with a comprehensive clinical review by its pharmacy and therapeutics committee to evaluate its utilization management criteria and formulary placement. And while it is encouraged that the FDA approved Zarxio prior to finalizing any guidance regarding interchangeability, Catamaran "would like to see interchangeability for biosimilars in order to facilitate appropriate substitution, which will improve adoption and savings,"

remarks Sumit Dutta, M.D., senior vice president and chief medical officer.

In the short term, payers are still waiting for Zarxio to officially launch, which has been delayed by Neupogen maker Amgen's request for a preliminary injunction to permit its sales, the latest step in a lawsuit the company filed in November. As a result, Sandoz has agreed to temporarily delay its launch of Zarxio until as late as April 10.

Stettin adds that it's impossible to formulate a "complete strategy" until the drug comes to market, but that payers "should be thinking about the formulary positioning of the drugs and they should expect that when there is more than one drug competing in the same category and has the same indication and same use and same safety profile, that they should have plans in place to drive utilization to the product that offers the best value for patients and their plan."

"As far as what the market ultimately delivers for interchangeability, I think it's going to be driven off of price at the end of the day," suggests DeNucci. "If these products aren't significantly cheaper, no one's going to make headway to get them into the market place."

The second major issue is provider and pharmacy/medical community barriers, points out DeNucci. "Are there perceived barriers due to the naming, whether they are biosimilar or interchangeable biosimilar? Those two things are really going to drive the uptake of these products," he suggests.

Langley predicts that the adoption curve for Zarxio may be slow compared with some other future biosimilar approvals. "Of all the different therapy classes, because of the underlying distribution channel and reimbursement fundamentals, I don't think it's going to gain a particularly large share of the marketplace" he added. "And PBMs are only going to be able to increase adoption of Neupogen on the increment, to the extent to which
Neupogen would go through the pharmacy benefit."

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