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Will State Action on Biosimilars Thwart Anticipated Savings for Private and Government Health Care Programs?



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Government and private health-care program payers have been anxiously awaiting FDA action on biosimilars. Payers anticipate that the ability to substitute and dispense a biosimilar product in lieu of a more expensive prescribed biologic or specialty drug may save payment programs millions, if not billions, of dollars.

In order to freely substitute a biosimilar for a prescribed reference biological product, the FDA must determine that the biosimilar is interchangeable with the reference product.

Interchangeability is a rigorous clinical standard to meet. The data must show that the biosimilar can be expected to produce the same clinical result as its reference product in any given patient and that the risk of switching between the biosimilar and its reference product is not greater than the risk of maintaining the patient on the reference product.

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On March 6, 2015, the FDA approved the first biosimilar under the abbreviated approval pathway created by the Affordable Care Act's amendments to the Public Health Service Act.[1] The FDA deemed Sandoz's product Zarxio to be a biosimilar of the reference cancer drug Neupogen (filgrastim) and approved Zarxio for the same indications as Neupogen.

Sandoz did not, however, seek approval to market Zarxio as interchangeable with Neupogen, perhaps because the FDA has yet to provide substantive guidance on the standards it will use to determine biosimilar interchangeability.

Therefore, as a practical matter, physicians will have to specifically prescribe Zarxio (filgrastim-sndz) if they want a patient to receive the biosimilar product.[2] Zarxio, and any other future biosimilars that are not approved as interchangeable, cannot be dispensed automatically as a substitute for the prescribed reference product.[3]

[1] These amendments are also called the Biologics Price Competition and Innovation Act of 2009 (BPCIA), which created new PHS section 351(k).

[2] The ''filgrastim-sndz'' nonproprietary name for Zarxio is temporary until the FDA completes its policy on biosimilar naming, which is expected to be released by the end of 2015, according to a late April update to the agency's list of planned draft guidance documents.

[3] As of May 15, Zarxio was not yet being marketed due to ongoing litigation between Sandoz and the manufacturer of the reference filgrastim product, Amgen. Sandoz had agreed not to begin distribution of the product until May 11, 2015, but

Despite the lack of FDA guidance on interchangeability, federal and state government entities are attempting to get ahead of the biosimilar curve by establishing biosimilar reimbursement and substitution policies. On March 30, 2015, CMS released guidance addressing Medicare and Medicaid coverage and reimbursement of FDA-approved biosimilar drug products.

At the same time, multiple states have enacted, or are considering, legislation that would impose procedural hurdles to the substitution of biosimilars for prescribed reference drug products.

Medicare Reimbursement Guidance

In its initial action on biosimilars, CMS issued two Medicare-related documents: (i) guidance on Medicare Part B reimbursement of outpatient provider-administered drugs, and (ii) guidance on Medicare Part D reimbursement for outpatient self-administered drugs.[4]

Under Medicare Part B, CMS directly reimburses health-care providers for the average cost of the drug the provider administers to a Medicare beneficiary in an outpatient setting.

In 2005, the Part B reimbursement methodology changed significantly from one based on purchase price to one based on market-centered price measures, or Average Sales Price (ASP). ASP is defined as the volume-weighted average manufacturer sales price net of price concessions to U.S. purchasers and excluding sales to other purchasers and sales that are exempt from Medicaid ''best price'' calculations.[5]

For purposes of determining ASP, pharmaceutical manufacturers must report their ASP for each drug to CMS. CMS, in turn, reimburses providers for Part B administered drugs using the reported ASP for the drug plus a 6 percent margin to cover the provider's overhead costs.[6]

CMS's Medicare Part B guidance on biosimilars notifies health care professionals that:

■ CMS intends to create distinct reimbursement codes for approved biosimilars to distinguish the biosimilar from the reference product. For the one approved biosimilar, CMS anticipates including a code for it in the coming weeks, retroactive to the FDA approval date. Because the biosimilar will have its own reimbursement code, it will have its own ASP.

■ Medicare Part B reimbursement to health care providers for biosimilars will use the ASP, with a twist. Once the manufacturer's Wholesale Acquisition Price (WAC) is available for the biosimilar, Medicare will pay 106 percent of the WAC before transitioning to payment based on 100 percent of the ASP of the biosimilar, but the 6 percent ''overhead'' cost will not be based on 6 percent of the biosmilar's ASP but on 6 percent of *the ASP for the reference product*.

Through this reimbursement formula, health care providers will, in theory, have no financial incentive to use the more expensive reference product. The 6 percent reimbursement retained by the provider will be the same whether the brand reference drug is used or the biosimilar is used. Medicare, in turn, will realize savings from use of the biosimilar through reduced payment (i.e. ASP) for the actual drug.

Importantly, Medicare's Part B reimbursement guidance is specific to reimbursement for *health-care professionals*. The materials are silent on Part B reimbursement for hospital outpatient use of biosimilars.

With respect to Medicare Part D reimbursement for self-administered biosimilars, CMS addresses several basic, but key issues for Part D plans:

■ A biosimilar and a reference product will *not* qualify as different drugs for purpose of satisfying CMS's regulatory requirements on formulary drug access.[7]

■ The addition of a biosimilar and removal of the reference drug from a formulary will be considered a non-maintenance change, to be evaluated on a case-by-case basis.

■ Because biosimilars are not automatically interchangeable with the reference drug, CMS expects Part D Plan Sponsors' Pharmacy & Therapeutics (P&T) committees to review newly approved biosimilars under the Part D Drug Benefit Manual, Chapter 6, § 30.1.5.

■ For purposes of Part D transition supplies, biosimilars and the reference product should be treated as different products.

■ Biosimilars do *not* meet the CMS definition of generics or multi-source drugs and therefore are to be treated as brand products for reimbursement. This means that biosimilars are subject to the higher maximum copayments for low-income subsidy (LIS) eligible individuals.

■ Biosimilars are non-applicable drugs when it comes to the Part D Coverage Gap Discount Program and are not otherwise subject to the requirements of that program.

Medicaid Requirements and Recommendations

With respect to the Medicaid Drug Rebate Program, CMS has determined that biosimilars fall under the definition of a single-source drug and will be subject to calculation of Unit Rebate Amounts and payment of rebates at the same rates as single source drugs.[8]

Although state Medicaid programs will likely set individual state regulatory or programmatic requirements for coverage of biosimilars, CMS is looking to encourage states and Medicaid Managed Care Plans to maximize the potential cost savings that may be achieved through use of biosimilars.

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a federal injunction issued on May 5 has furthered delayed the Zarxio launch.

[4] *See* http://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNMattersArticles/Downloads/SE1509.pdf, and https://www.pharmamedtechbi.com/~/media/Supporting%20Documents/The%20Pink%20Sheet%20DAILY/2015/March/Part%20D%20biosimilars.pdf.

[5] 42 U.S.C. § 1395w-3a(c).

[6] 42 C.F.R. § 405.

[7] 42 C.F.R. § 423.120.

[8] *See* https://www.pharmamedtechbi.com/~/media/Supporting%20Documents/The%20Pink%20Sheet%20DAILY/2015/March/Medicaid%20biosimilars.pdf.

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Therefore, CMS recommends that:

■ States should consider adding biosimilars to state supplemental rebate programs.

■ States and Medicaid Managed Care Plans should consider using Drug Utilization Review (DUR) and state P&T Committees to educate physicians and pharmacists on appropriate prescribing and dispensing of biosimilars.

■ States and Medicaid Managed Care Plans should consider educating prescribers and pharmacists on biosimilars through electronic prescribing messaging and point of sale (POS) edits.

State Legislative Action

Although the federal government is optimistic about the potential cost-savings from biosimilars, state legislation that imposes conditions on when an FDA-approved *interchangeable* biosimilar can be substituted for a prescribed reference drug may frustrate expected program savings.

According to the National Conference of State Legislatures, as of the end of April 2015, there were at least 39 bills or resolutions filed in 23 states related to biologics and/or biosimilars. In addition, 10 states have enacted legislation on the subject[9]; even more recently, in Georgia a biosimilar substation bill was signed by the governor on May 6, 2015. Moreover, at least one state Board of Pharmacy has taken action on biosimilar substitution by proposing an amendment to the regulations governing the practice of pharmacy.

These emerging state laws address the circumstances under which a pharmacist may substitute an FDA-approved interchangeable biosimilar for the prescribed biologic. Most of these state statutes focus on the type of notice required for substitution of an interchangeable biosimilar by a pharmacist, such as who must be notified of the substitution, and also when and how that notice must be conveyed.

Given there are as of yet no biosimilar drugs approved as interchangeable, the state statutes may be viewed as hypothetical in nature. But determinations of interchangeability are bound to happen after FDA clearly articulates the standards that Section 351(k) applicants must meet in order to market an interchangeable biosimilar.

Pharmacies, PBMs, and payors will want to be cognizant of the applicable limits and conditions imposed on pharmacy substitution in the various states.

For example, the newly enacted Colorado law[10] permits a pharmacist to substitute a biosimilar for the prescribed reference product if:

■ the FDA has approved the biosimilar drug as interchangeable with its reference product;

■ the prescriber has not conveyed a limit on substitution to the pharmacist by one of the methods set out in the statute;

■ the substituted product will cost the purchaser less than the prescribed product; and

■ the pharmacist communicates the substitution to the purchaser in writing and orally, labelling both the container and the prescription accordingly.

Like the Colorado law, other state biosimilar substitution laws address whether a prescriber must be notified of a substitution and how and when that notice is conveyed. Many laws also establish requirements for recordkeeping at the pharmacy level. The requirements vary considerably from state to state.

For example:

1. The recently passed Georgia law [11] requires a pharmacist to communicate to the prescriber within 48 hours the name and manufacturer of a dispensed biological product. This notice requirement appears to apply regardless of whether a reference biological product or a biosimilar product is dispensed. The requirement is waived in situations where there is no FDA-approved interchangeable biosimilar. Substitution of an interchangeable biosimilar is permitted as long as the biosimilar has a lower price than the reference product, and the prescriber has not indicated ''brand necessary'' in the prescription.

2. Massachusetts's biosimilar substitution law [12] allows a pharmacist to substitute an interchangeable biosimilar product for the prescribed reference product unless the prescriber has instructed otherwise in writing specific to the patient. Nevertheless, the pharmacist must notify the prescriber of the substitution ''within a reasonable time'' after making the substitution through one of the specifically prescribed methods.

3. Indiana's biosimilar substitution law [13] permits a pharmacist to substitute an interchangeable biosimilar product only if the prescriber has indicated ''may substitute'' on the prescription and the pharmacist informs the customer of the substitution.

4. Florida's biosimilar substitution law [14] allows the pharmacist to dispense an interchangeable biosimilar for the reference product unless the prescriber has expressed a preference against substitution. However, the pharmacist must notify the person submitting the prescription of the substitution, the price differential between the biosimilar and the reference product, and their right to refuse the substitution.

5. Utah recently amended its biosimilar substitution law [15] to extend the time period for the dispensing pharmacist or his/her designee to record the biosimilar substitution, but the amendment left in place requirements that the purchaser request/consent to the substitution as well as requirements specific to out-of-state mail order pharmacies providing biosimilar drugs to patients in the state.

These statutes have yet to be implemented, but challenges are already apparent:

■ Certain pharmacist professional associations have objected to the notification requirements included in

[9] http://www.ncsl.org/research/health/state-laws-and-legislation-related-to-biologic-medications-and-substitution-of-biosimilars.aspx

[10] Senate Bill 15-071 (2015), codified at Colo.Rev.Stat. § 12-42.5-102(3.7), (13.5) and (16.5).

[11] S.B. 51 (A/P signed May 6, 2015).

[12] Mass.Gen.Law. ch.112, § 12EE.

[13] Ind.Code § 16-42-25.

[14] Fla.Stat.§ 465.0252.

[15] Utah Code § 58-17b-605.5.

most state biosimilar substitution laws. The Academy of Managed Care Pharmacy has argued that these notification requirements are burdensome and may in fact discourage biosimilar substitution.

■ Most of the statutes are under the auspices of the state's Board of Pharmacy and address information that must be provided by a pharmacist looking to substitute a biosimilar for a prescribed self-administered reference biological product. But in all likelihood, many biosimilars will be provider-administered, not self-administered—and the statutes do not address what, if any, notice a health care provider must provide a patient before that provider decides to administer a biosimilar instead of the reference product.

■ Multiple statutes use varying language to establish requirements for what the pharmacist must convey to the ''purchaser'' or ''customer'' or ''patient.'' But in the context of filling a prescription at a pharmacy, there are many variables that may come into play. For example, when there is a Medicaid-covered beneficiary with no co-pay, who is the purchaser: Medicaid or the Medicaid beneficiary? If a patient has their spouse submit/pick up the prescription, will providing the notice to the spouse suffice for notifying the ''patient''? What if it is not a spouse but a friend—what information can be conveyed to that individual to meet statutory requirements but not violate patient privacy protections? What if the patient is an infant?

■ These statutes all pre-date state Medicaid program consideration of biosimilar substitution. What if the Medicaid program adopts mandatory biosimilar substitution regulations as a cost-saver—will those regulations trump the pharmacy-based statutes?

What's on the Horizon?

Payors, including government programs, want to embrace biosimilars and encourage their use in order to reap the cost-saving benefits. But it is obvious from the federal and state governments' first steps in this area that complications abound. When it comes to Medicare's treatment of biosimilars, CMS's initial position on how to view the biosimilar appears to be ''it depends.''

For now Medicare *will not* treat a biosimilar as a different drug from the reference product when it comes to meeting drug access requirements and LIS discounts, but *will* treat the biosimilar as a different drug from the reference drug when it comes to other reimbursement issues, such as transition fills and P&T approval.

Perhaps taking its cue from the FDA, CMS's biosimilar guidance documents should be viewed as a first step: historic in some aspects, but at the same time tentative and incomplete.

State legislators and regulators also are considering the future of biosimilars. As with CMS (and the FDA, which has been criticized for the ''slow'' or ''cautious'' way it is implementing the BPCIA), the states' initial attempts at legislation appear to be tentative and incomplete. Whether the individual state requirements can actually be implemented may have to wait on the actual entry of an interchangeable biosimilar into the marketplace.

But among all these questions, one thing is clear: biosimilars are coming and industry stakeholders should keep an eye out for rapidly evolving developments on both the federal and state levels.

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