BNA

Pharmaceutical Law & Industry Report®

Where Will Biosimilars Fit in Federal Drug Pricing Programs?

By Donna Lee Yesner

When Congress amended section 351 of the Public Health Service Act in 2010 to create a new abbreviated pathway for approving biosimilar biologic products, as had been created earlier for generic versions of pioneer drugs, it clearly wanted to create economic incentives for manufacturers to develop these products. For example, it created a process for establishing a reference biological product against which the applicant biosimilar product would be evaluated, and an exclusivity period, as it had done for generic companies under the Hatch-Waxman Act, though the provisions are dissimilar. It also excluded biological products approved under the new licensing authority from certain new burdens imposed on manufacturers of pioneer biologics. Unfortunately, no similar consideration was given to the treatment of this new category of biologics under drug pricing laws and regulations, and the impact this treatment will have on the price paid for these products. In short, Congress simply failed to address how the various federal programs that currently differentiate between innovator and generic drugs will accommodate a new category of biological products. Yet, how biosimilars are categorized can have significant reporting and financial consequences.

Donna Lee Yesner is a partner in the FDA & Healthcare practice at Morgan, Lewis & Bockius LLP, resident in the firm's Washington office. She also is a member of the advisory board for BNA's ***Pharmaceutical Law & Industry Report.*** *She would like to acknowledge FDA & Healthcare partners Andrew Ruskin and Stephen Ruscus for their contributions to this article.*

Biosimilars and Medicare Part B

As a general rule, biological products are administered to Medicare patients by physicians in clinical settings, and are reimbursed by Medicare Part B, rather than under the Part D pharmacy benefit. Pursuant to the Medicare Modernization Act, physicians are paid for ''single source drugs and biologicals'' based on 106% of the lower of the Average Sales Price (''ASP'') or the Wholesale Acquisition Cost for all National Drug Codes assigned to the product using the methodology for calculating ASP for multiple source drugs. That methodology yields a volume-weighted average of the average sales prices reported to the Centers for Medicare & Medicaid Services (''CMS'') for all the National Drug Codes assigned to all drugs within the same drug billing and payment code. The statute does not seem to permit payment for biological products based on a volume-weighted average of multiple products, nor does it define biological product as one for which there is a single source. *See* Social Security Act section 1847A(b)(4),(6). Further, it has been CMS policy to assign unique billing codes to biological products. Accordingly, the only averaging of prices across biological products occurs within the product family sharing the same billing code.

Because Congress did not differentiate between a reference biological product approved under subsection 351(a) of the Public Health Service Act and a biosimilar biological product approved under new subsection

 ISSN 1542-9547

351(k) in connection with Medicare Part B, use of the term ''biological product'' raises questions as to how biological products approved under the new pathway will be reimbursed under Part B. As noted, a literal reading of the statute requires payment of a discrete biological product identified in the U.S. Pharmacopia (except those sharing a billing code before October 1, 2003) as a ''single source drug or biological'' and not as a ''multiple source drug.'' Even if CMS has discretion with respect to its assignment of billing codes to biosimilars, and authority to pay providers for biological products differently than single source drugs if there are approved biosimilars on the market, it must deal with the issue of interchangeability.

Under Medicare Part B, a drug product must meet strict statutory criteria to qualify as a multiple source drug and be subject to the weighted average ASP for multiple source drugs. The drug must be rated pharmaceutically equivalent and bioequivalent by the Food and Drug Administration (''FDA''). Even if two drugs are bioequivalent, to be pharmaceutically equivalent, they must contain identical amounts of the same active ingredient in the same dosage form and meet certain other standards. At this point, it is unclear what standards for interchangeability will be applied to biological products approved under subsection 351(k) and what standards will apply for purposes of payment under Part B. Biosimilar biological products may be licensed under subsection 351(k) even if they do not meet the FDA's eventual standard for interchangeability and are deemed to have a new active ingredient, making the coding decision even more subjective. The consequences are significant.

If a biosimilar biological product shares the same billing code with the reference biological product, the presumably lower sales prices of the biosimilar product will be factored into the weighted ASP paid a physician for either product. By doing so, CMS would increase the physician's margin on lower-priced biosimilar products, thereby creating an incentive to purchase them, and would simultaneously create an incentive for pioneer reference biological manufacturers to lower their sales prices in order to reduce the reimbursement differential and reduce loss of market share. At the same time, the payment structure would penalize doctors and their patients if the higher priced pioneer biological product is more effective for that patient.

The same problems of downward pricing pressure on manufacturers and pressure on providers to administer the least costly alternative also apply to biosimilars approved under subsection 351(k) that are different from other biosimilars referencing the same innovator product and which might have therapeutic advantages but cost more to develop and manufacture because of their dissimilarities. If biosimilars are treated the same as multiple source drugs, experience with payment provisions for these drugs could threaten investment in new biological products and reduce the incentives for at least some pioneer companies from bringing them to market. Before subjecting biosimilars to one-size-fits-all Medicare payment rates, clear standards are needed to determine the extent to which biological products are similar and interchangeable.

Biosimilars and the Medicaid Drug Pricing Program

The Medicaid Drug Rebate Program (section 1927 of the Social Security Act, codified at 42 U.S.C. 1396r-8), was established to reduce the cost to Medicaid of prescription drugs dispensed or administered to beneficiaries in the outpatient setting. The program requires manufacturers to enter into an agreement with Department of Health and Human Services (''HHS'') to report certain pricing information to the federal government, and pay rebates to the states on covered outpatient drugs as a condition for provider reimbursement by the Medicaid program. Manufacturers' obligations under the statute and the rebate agreement differ depending on whether the product is classified as a ''single source drug,'' an ''innovator multiple source drug,'' or an ''other drug'' (*i.e.*, a covered outpatient drug other than a single source drug or an innovator multiple source drug). With few exceptions, single source drugs and innovator multiple source drugs are subject to a rebate formula based on a minimum 23.1% of the drug's Average Manufacturer Price (''AMP'') or the difference between AMP and the drug's best price, plus an additional rebate penalty based on increases in AMP over the Consumer Price Index-Urban since product launch. If a product's commercial price increases over this benchmark for any reason, including ingredient costs, the penalty applies and the total rebate can equal the drug's AMP, meaning the manufacturer must in effect rebate the amount it received on the sale. By contrast, covered drugs that do not fit into these two categories are subject to a different formula based on a lower percentage of AMP (13%) with no inflation penalty. Accordingly, manufacturers of single source drugs and innovator multiple source drugs must calculate and submit the best price for the drug as well as the AMP each quarter and pay the states a much higher rebate amount.

The rebate statute defines ''single source drug'' as a drug ''produced or distributed under an original new drug application (NDA) approved by the Food and Drug Administration, including a drug product marketed by any cross-licensed producers or distributors operating under the new drug application.'' The term ''innovator multiple source drug'' means a multiple source drug that was originally marketed under an original NDA approved by the Food and Drug Administration. For a drug to be considered a multiple source drug, there must be two or more products rated as therapeutically equivalent, and they must be pharmaceutically equivalent, meaning they must contain the same active pharmaceutical ingredient in the same dosage form. In the Deficit Reduction Act of 2005, Congress again imposed distinct drug pricing obligations on manufacturers based on whether the drug was approved for sale under section 505(c) of the Federal Food, Drug, and Cosmetic Act (''FFDCA''). Thus, historically, a manufacturer's obligations under the Medicaid drug rebate program turned on whether the drug was marketed under section 505(c) (for NDAs) or 505(j) (for abbreviated new drug applications) of the FFDCA.

In 1990, when the Medicaid drug rebate program was established, it covered both pharmaceutical products approved under sections 505 and 507 of the FFDCA, including generic drugs approved under section 505(j), and biological products (other than vaccines) licensed under section 351 of the Public Health Service Act,

  PLIR ISSN 1542-9547

which would encompass the new abbreviated biologics license application (ABLA) process under subsection 351(k) for biosimilars. However, unlike the Medicare ASP provisions, the Medicaid drug rebate statute did not include biological products approved under a licensing authority in the provisions establishing the applicable rebate formula or the definition of ''single source drug'' or ''innovator multiple source drug.'' As biological products were considered unique products and had only a single source, by regulation, CMS included in the definition of ''single source drug'' any ''covered outpatient drug approved under a biological license application [BLA],'' rather than including such a product in the catchall term ''other drugs.''

Under subsection 351(k), biosimilars are approved under a new abbreviated process for licensure of biological products, not the original biologic license application (BLA) process, and it appears Congress intended that they be considered similarly to drugs undergoing the abbreviated new drug application (ANDA) process authorized by section 505(j) of the FFDCA. However, as Congress failed to address the classification of biological products under the Medicaid statute, it is unclear whether licensure of biosimilars under section 351(k) triggers different obligations than those applicable to biological products licensed under subsection 351(a). Is the licensure process contemplated by section 351(k) excluded from the term ''biological license application'' as used in the CMS regulations? Does it matter if the approved biosimilar is determined to be non-interchangeable, and thus could be considered under the Medicaid statute to be a ''new'' active ingredient? If biosimilars are neither biological products approved under a BLA nor innovator multiple source drugs, it appears they are, by default, within the category of ''other drugs.'' If not, the manufacturer of a biosimilar would have to calculate and submit a best price, would be penalized for increasing the product's prices after launch, and would remit a higher rebate amount on the sale. If they are categorized as ''other drugs,'' the manufacturer would have fewer reporting obligations and could retain a higher percentage of the drug's selling price, while the states would receive considerably smaller rebates.

If a product approved under section 351(k) is not considered to be approved under a BLA, and thus is not classified as a single source drug, there is an additional issue of whether such a product meets the definition of a multiple source drug. Under the current Medicaid statute definition of ''multiple source drug,'' a biosimilar could not be a multiple source drug if the active ingredients are not identical in dosage form. As additional biosimilars come on the market, this issue is important because Medicaid not only collects rebates on drugs administered by physicians in the outpatient setting, it also sets an upper limit on the amount states may pay providers for multiple source drugs, including both the pioneer drug and generic versions of the drug, if there are three products on the market that meet the multiple source drug definition. If biosimilars are considered ''multiple source drugs'' under the program, they would presumably be subject to the same payment cap. On the other hand, if biosimilars are neither single source drugs nor multiple source drugs, the manufacturer of the biosimilar would pay the lower rebate for ''other drugs'' while avoiding an upper payment limit, and the pioneer reference biological product would remain a single source drug not subject to a payment cap.

340B Program

The issues that affect rebate payment obligations under the Medicaid drug rebate statute also affect the purchase price manufacturers charge under the 340B program. This program, named for section 340B of the Public Health Service Act, conditions Medicaid coverage of outpatient drugs on execution of a different contract by manufacturers and HHS. The 340B pharmaceutical pricing agreement requires manufacturers to charge certain federal grantees no more than the price specified in the statute, which is derived from the Medicaid rebate formula, *i.e.*, AMP reduced by the Medicaid rebate percentage, for drugs covered by the Medicaid rebate program. Consequently, if the rebate amount for a biosimilar is based on the higher percentage of AMP applicable to single source drugs and innovator multiple source drugs, rather than the percentage applicable to ''other drugs,'' the 340B discount will be correspondingly greater. Moreover, the inflation penalty would apply which, when triggered, would enable the program participants to purchase the products at a very low price. Because these purchasers resell 340B drugs to their patients' health plans at the plans' normal reimbursement rate, they would benefit more from treatment of biosimilars in the same manner as products approved under a BLA.

Veterans Health Care Act Procurements

The same statute—the Veterans Health Care Act—that conditions Medicaid coverage on an agreement to cap prices to participants in the 340B program, also conditions Medicaid coverage on manufacturers having a pricing agreement with the Department of Veterans Affairs (''VA''), called a Master Agreement. Under this agreement, manufacturers promise to offer their products for sale to four federal agencies on the Federal Supply Schedule and to charge no more than a discounted price based on a statutory formula. The Federal Ceiling Price is 76% of the Non-Federal Average Manufacturer Price, which is a distinct calculation from the AMP used in determining rebate amounts in the Medicaid program. The Veterans Health Care Act and Master Agreement cover single source drugs and innovator multiple source drugs as defined in the Medicaid statute and, in addition, cover ''any biological product identified under section 600.3 of title 21, Code of Federal Regulations.'' This section of the CFR broadly describes biological products without reference to the FDA approval process. A biosimilar is still a biological product under section 600.3 of title 21. Indeed, vaccines, which are essentially interchangeable biological products, have always been treated by the VA as covered drugs even though they are expressly exempt from the Medicaid drug rebate program. Thus, it is likely that the VA will consider products approved under subsection 351(k) that meet the definition of a biological product under 21 C.F.R. 600.3 to be subject to the Veterans Health Care Act requirements. In that event, the biosimilar manufacturer must calculate and submit drug pricing in compliance with the statute and contract with the VA to sell the product to the VA and other eligible agencies at the Federal Ceiling Price.

Medicare Part D Coverage Gap Discount

Medicare Part D is implemented through commercial health plans that negotiate with manufacturers to receive rebates on prescriptions dispensed by retail pharmacies and covered by the plans. As currently structured, Part D Plans provide coverage over the deductible amount up to a certain limit and then resume coverage once the next threshold has been met. While a Medicare beneficiary is in this coverage gap, also known as the ''donut hole,'' the plan is not responsible for any of the prescription cost. In order to alleviate the burden on beneficiaries, the health care reform law created a new program which made coverage by Medicare Part D Plans contingent on agreements with manufacturers of applicable drugs to discount the price paid by beneficiaries in the donut hole by 50%. Unlike programs that pre-dated health care reform, this program took the new biosimilar approval pathway into account and expressly excluded biological products licensed under subsection 351(k).

Tax on Government Sales

In addition to all the various discounts and rebates that must be provided on biological products approved under a BLA, health care reform legislation imposed a tax on sales of branded drugs to the federal government, including sales to providers reimbursed by federal health care programs. As with the coverage gap discount required by the same legislation, this provision is limited to biological products licensed under subsection 351(a) of the Public Health Service Act. Although the tax is computed on actual sales dollars net of discounts and rebates, the aggregate effect of an allocated share of the tax reduces the net realization on the sale of a covered drug. Thus, for example, if a biological product licensed under subsection 351(a) is sold to VA facilities under the Federal Supply Schedule, the prices are not only capped, but the realization on the sale is reduced by the tax, whereas biosimilars, even if subject to the Federal Ceiling Price, would not be subject to the tax. Similarly, if a 351(a) product were sold to a 340B provider for outpatient treatment of a Medicare-covered patient, and it is covered by Part D, the product would be subject to a 340B program purchase discount, potentially another discount to the plan and the patient if the unit is dispensed during the coverage gap, and a tax on the sale of the unit. By contrast, the same sale of a biological product approved under subsection (k), would be subject to the 340B drug discount (with the amount determined by how it is classified under the Medicaid statute), but not the Medicare coverage gap discount or the tax on federal sales, even if the product was not interchangeable and had a new active ingredient.

Summary

The new pathway for approving biosimilars raises many questions as to how these products should be treated under federal drug pricing laws, and though biosimilars have been excluded from some newly created programs, it is risky for manufacturers to assume their legal obligations are the same as if biosimilars are the equivalent of generic drugs for these pricing and reimbursement purposes. Hopefully, CMS and the VA will not wait until the first biosimilars are approved to take action necessary to remove uncertainties and the risk of noncompliance with statutory drug pricing provisions applicable to biological products approved under section 351.

PLIR ISSN 1542-9547