THORN RUN PARTNERS
GOVERNMENT RELATIONS

Background Brief: BPCIA

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SUBJECT: Status of Biosimilars Implementation

I. EXECUTIVE SUMMARY

This memorandum provides background on the Food and Drug Administration's (FDA's) implementation of the Biologics Price Competition and Innovation Act's (BPCIA) abbreviated licensure pathway for products that are biosimilar to – or interchangeable with – a licensed biologic reference product.[1] After a lengthy wait for implementing guidance, key pieces of which remain pending, biosimilars implementation has begun to accelerate. The FDA and Centers for Medicare and Medicaid Services' (CMS) policy on biosimilars naming, reimbursement and other areas will significantly affect both biosimilar and innovator therapies as it is codified. States also are wading into biosimilars policy with varying policy objectives, including easing biosimilar adoption or curtailing unwanted switching among therapies.[2]

II. FDA GUIDANCE: WHAT'S IN PLACE AND PENDING?

The following chart depicts key guidance that has been released along with highly anticipated documents that remain forthcoming:

CMS and FDA Guidance: Issued and Expected Documents

Topic	Status	Proposals/Guidance
Naming	• Draft guidance released on Aug. 28[3]; comments due by Oct. 27[4] • Parallel proposed rule applies draft naming convention to six previously licensed products; comments due by Nov. 12[5]	• Common core name derived from drug substance with distinguishable unique suffix that is devoid of "meaning" o Comment sought on other approaches (e.g., deriving suffix from name of license holder) o Core name and distinguishable (meaningless) suffix applicable to interchangeable products, though comment sought on potential for same names

[1] ACA Section 7002, summarized at Healthcare Lighthouse here.
[2] National Council of State Legislatures (NCSL) website, accessed Sept. 10, 2015, available here.
[3] FDA, Nonproprietary Naming of Biological Products, Aug. 28, 2015, available here.
[4] 80 *Federal Register* No. 167, p. 52296, available here.
[5] 80 *Federal Register* No. 167, p. 52224, available here.

Medicaid Rebates	• Guidance issued on March 30[6]	• Biosimilars defined as single-source drugs with rebates applicable in same manner as reference (brand) biologic
Medicare Part D Coverage	• Guidance issued on March 30[7]	• Biosimilars not considered different than reference biologic for purposes of satisfying two distinct drug requirement in each Part D-covered class o May be added to Part D formularies as enhancement at any time o Considered non-maintenance change if biosimilar is replacing reference biologic • Biosimilars to be evaluated by P&T committees within specified timetables if not interchangeable • Biosimilars treated as a different product than reference biologic for purposes of transitional fills • Biosimilars not yet addressed in context of Part D protected class requirements[8]
Medicare Part B Coding/ Reimbursement	• Issued in 2016 Physician Fee Schedule proposed rule[9] • Final rule expected in November	• All biosimilars referencing same innovator biologic grouped under same HCPCS code • Payment based on weighted average of those biosimilars plus six percent of the reference biologic's ASP
Hospital OPPS Coding/ Reimbursement	• Issued in 2016 Hospital Outpatient Prospective Payment System proposed rule[10] • Final rule expected in November	• ASP plus six percent • Coding follows Medicare Physician Fee Schedule proposal (see above)
Interchangeability	• Not yet released	• Expected by end of 2015[11] • Recently cited as "on track" by FDA with the caveat that multiple clearances are involved[12]
Labeling	• Not yet released	• Expected by the end of 2015[13] • Process includes review of stakeholder input, including an AbbVie citizen petition [14] that requests clear identification of a product as a biosimilar and specification that a product is not interchangeable unless the FDA has determined it to be interchangeable

[6] CMS, Medicaid Drug Rebate Program Notice Release No. 169, March 30, 2015, available here.
[7] *Inside Health Policy*, March 2015.
[8] Avalere, Alliance for Health Reform panel, May 2015, available here.
[9] CY 2016 Medicare Physician Fee Schedule proposed rule, July 8, 2015, available here.
[10] CY 2016 Hospital Outpatient Prospective Payment System proposed rule, July 15, 2015, available here.
[11] FDA Center for Drug Evaluation and Research, 2015 Guidance Agenda, April 28, 2015, available here.
[12] Janet Woodcock, Testimony before the Senate Health, Education, Labor and Pensions Subcommittee on Primary Health and Retirement Security, Sept. 17, 2015, archived here.
[13] *Ibid*.
[14] AbbVie statement, June 3, 2015, available here; Woodcock testimony, Sept. 17, 2015.

Data Extrapolation; Statistical Approaches	• Not yet released	• Expected within six months[15]

Interchanegability

While the FDA has released draft guidance on naming, which includes reference to naming policies for interchangeable biosimilar products, the policy for identifying products as interchangeable has not yet been issued. The agency has released select FAQs on the interchangeability process[16] without yet fully delineating the bar for attaining this critical category. Members said at a Sept. 17, 2015, Senate hearing [17] on biosimilars implementation that interchangeability is a top priority for FDA guidance and urged the agency to release such guidance as soon as possible. Sen. Bill Cassidy (R-LA) emphasized the nuanced considerations of defining interchangeability, which he said is the "highest bar" of biosimilarity. He noted, for example, that even determining biosimilarity is challenging because two lots of the reference product may not be fully identical, given that biologics are derived from living organisms and therefore are more challenging to manufacture than small-molecule drugs.

Dr. Janet Woodcock, director of the FDA's Center for Drug Evaluation and Research, said that the agency believes it is "scientifically and practically feasible" to demonstrate interchangeability and that "we're going to get there."[18] She elaborated on the complexities of making such determinations. For example, she noted the role of human immune response produced by biologic and biosimilar medicines, presenting the question of whether continued switching could boost immunity and result in "untoward effects," she said. Dr. Woodcock cited an example in which differences in a reference product – erythropoietin – resulted in pure red cell aplasia and caused dependence on blood transfusions. [19] Presaging potential issues that could be addressed in draft interchangeability guidance, she noted that similarity at a "fingerprint" level would be a strong point in favor of biosimilarity and interchangeability, although she added that small manufacturing changes – even in a reference product – could have an impact on immune response.

[15] Woodcock testimony, Sept. 17, 2015.
[16] FDA, Biosimilars Questions and Answers Regarding Implementation of the BPCIA of 2009, April 2015, available here.
[17] Senate Health, Education, Labor and Pensions Subcommittee on Primary Health and Retirement Security, Hearing: "Biosimilars Implementation: A Progress Report from the FDA," Sept. 17, 2015, archived here.
[18] Woodcock testimony, Sept. 17, 2015.
[19] *Ibid*.

Additional Key Guidance

Guidance on biosimilar labeling is also highly anticipated. The FDA has cited "tradeoffs" in developing the guidance,[20] with key issues expected to include the extent to which labels must explicitly denote a product as a biosimilar and explain whether it has been deemed interchangeable with the reference product.

III. REIMBURSEMENT AND CODING ISSUES

Medicare Part B Coding

In March 2015, the FDA approved the first biosimilar, for Amgen's Neupogen (filgrastim). The biosimilar, Zarxio, is made by Novartis' Sandoz division.[21] In April 2015, CMS released a preliminary HCPCS code for Zarxio, which is different from the HCPCS code assigned to its reference product, and included it in a July 2015 update to Medicare Administrative Contractors. [22]

Under Medicare Part B, payment for physician-administered biologics in freestanding clinics (set by the Medicare Physician Fee Schedule (MPFS)) or in a hospital outpatient department (under the Hospital Outpatient Prospective Payment System (OPPS)) is determined by the Healthcare Common Procedure Coding System (HCPCS) code tied to the drug, with a crosswalk to the Ambulatory Payment Classification (APC) code when necessary.[23] Generally, for brand and generic drugs, CMS assigns the same HCPCS codes for drugs that are considered therapeutically equivalent (as listed in the FDA's Orange Book). By assigning a different HCPCS code for the biosimilar than for its reference product, CMS has diverged from that practice and created a distinguishable coding element for biosimilars.

Notably, CMS has assigned a temporary HCPCS "Q code," instead of a permanent HCPCS "J code," for Sandoz's filgrastim biosimilar. Temporary Q codes are assigned in cases when the agency does not have enough information to establish a permanent J code but still wants to make the drug available for claims processing. Commentators have observed that CMS may be awaiting the FDA guidance on interchangeability to a reference product, labeling for biosimilar products, and policies on appropriate naming conventions for biosimilar and interchangeable products.[24] By assigning a temporary Q code for filgrastim, CMS appears to have signaled that its approach is subject to change as policies evolve.

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[20] *Ibid*.
[21] FDA release, March 6, 2015, available here.
[22] CMS HCPCS agenda, May 7-8, 2015, available here; CMS transmittal, May 8, 2015, available here.
[23] CY 2016 Hospital Outpatient Prospective Payment System proposed rule, July 15, 2015, available here.
[24] Annemarie Wouters, "Biosimilars Coding & Reimbursement Significance under Medicare Part B," Manatt Health, June 16, 2015, available here.

Medicare Part B Reimbursement

Reimbursement for physician-administered biologics in a freestanding clinic statutorily is set at average sales price (ASP) plus six percent. The 2011 MPFS final rule implemented the statutory ASP plus six percent requirement for freestanding clinic reimbursement, which was reinforced by the 2016 MPFS proposal,[25] with some key amplifications detailed below.

In its 2016 proposed rule for the hospital OPPS, CMS clarified how it intends to reimburse for biosimilars administered in a hospital outpatient department. In that proposal, CMS said that it plans "to apply the same payment methodology that it uses for separately covered outpatient drugs (SCODs) and other biologicals to biosimilars."[26] This amount, CMS notes, "generally equates to average sales price (ASP) plus six percent." Until manufacturer ASP is available, CMS will pay 106 percent of the wholesale acquisition cost (WAC) of the product.

Pricing Considerations for Biosimilars with the Same Reference Biologic

In the 2016 MPFS proposal, CMS clarified that the payment amount for a biosimilar "is based on the ASP of all [National Drug Codes (NDCs)] assigned to the biosimilar biological products included within the same billing and payment code."[27] In effect, biosimilars referencing the same innovator biologic would receive the weighted average ASP of all others with the same reference product, with an additional six percent of the reference product's ASP added.[28] The 2016 hospital OPPS proposal integrates this strategy for ASP calculation for outpatient reimbursement. CMS notes, "We are proposing that HCPCS coding and modifiers for biosimilar biological products will be based on policy established under the CY 2016 MPFS rule."

A single HCPCS code may include multiple NDCs, with each NDC referring to different labelers (manufacturers), strengths, dosing, and packaging. The proposed ASP calculation does not include the prices for the underlying reference biologic, which has a separate HCPCS code and therefore a separate ASP calculation. The proposal essentially says that ASP for biosimilars for the same reference product would be based on the combined prices of all of the drugs contained within a given HCPCS code.

The decision to group all biosimilars for the same reference biologic under the same HCPCS code – only one biosimilar has been approved so none have been grouped together yet – has prompted some criticism from industry stakeholders that point to the potential for confusion.[29] It will be a crucial issue considered by the Administration during the comment period for the 2016 MPFS proposal. Stakeholders have expressed concern that the proposed payment approach is at odds with

[25] CY 2016 Medicare Physician Fee Schedule proposed rule, July 8, 2016, available here.
[26] CY 2016 Hospital Outpatient Prospective Payment System proposed rule, July 15, 2015, available here.
[27] *Ibid*.
[28] At one juncture in the House 21st Century Cures process, an offset was briefly considered but dropped that would have predicated ASP plus six percent on the biosimilar and not reference product ASP.
[29] Biosimilars Forum website, accessed July 9, 2015, available here.

distinguishable suffixes envisioned in the FDA's draft naming convention and the Medicaid rebate policy of treating biosimilars as single-source drugs. Members of Congress also weighed in, saying the reimbursement strategy treats biosimilars as generics and undermines the potential for a "vibrant" biosimilars market.[30]

MedPAC's Support for CMS' Proposal

The Medicare Payment Advisory Commission (MedPAC) has expressed support for CMS' proposal,[31] saying it could form the basis of policies that would reduce the price of both biosimilars and the brand biologics they reference. The Commission said the biosimilar industry's arguments against the policy are a means of seeking price protections, and the Commissioners suggested that drug makers should disclose their costs and revenues. Congress gave biologics 12 years of exclusivity in the ACA, and CMS hopes to drive down the price of biosimilars once that exclusivity period expires by placing biosimilars that reference the same brand biologics in single billing codes. Commissioners also said that if policymakers desire CMS claims data to complement the FDA's post-market monitoring, CMS could develop a way to distinguish biosimilars on claims without assigning them a unique code.

At the recent Senate HELP Subcommittee hearing, Dr. Woodcock confirmed that the FDA is working with CMS to develop such an approach.[32] She said that if CMS finalized the proposal to group biosimilars with the same reference product under a common HCPCS code, the agencies are developing sub-codes (e.g., modifiers) to "help distinguish who got what [biosimilar]" for safety monitoring purposes.[33]

Medicaid

On March 30, 2015, CMS issued guidance on biosimilars and the Medicaid Drug Rebate (MDR) Program.[34] In the guidance, CMS clarified that biosimilars fall within the definition of "single source drugs" for purposes of the MDR program. This means that manufacturers of biosimilars must pay rebates on state Medicaid utilization based on the rebate formula for branded drug products, not based on the rebate formula for generics.

In the guidance, CMS called the approval of biosimilar biological products "a unique opportunity to achieve measurable cost savings and greater beneficiary access to expensive therapeutic treatments for chronic conditions." [35] These savings, the agency suggests, may be achieved by states through "using the various drug utilization and cost management tools they have available (e.g., step therapy, prior authorization, preferred drug lists)," as well as through

[30] Anna Eshoo et al., Letter to CMS, Aug. 4, 2015, available on the Biosimilars Forum website here.
[31] Medicare Payment Advisory Commission, Comments to CMS on CY 2016 Medicare Physician Fee Schedule proposed rule, Sept. 8, 2015, available here.
[32] Woodcock testimony, Sept. 17, 2015.
[33] *Ibid*.
[34] CMS, Medicaid Drug Rebate Program Notice No. 92, March 30, 2015, available here.
[35] *Ibid*.

supplemental rebate agreements between states and manufacturers. Finally, to ensure "safe and efficacious use" of biosimilars, CMS encourages states to use drug utilization review programs and pharmacy and therapeutics (P&T) committees to inform physicians and pharmacists about appropriate prescribing and dispensing of biologics, including biosimilars.

IV. MARKET ENTRY

Although Zarxio was approved on March 6, 2015, it has become the subject of a legal dispute between Sandoz and Amgen, the maker of Zarxio's reference biologic Neupogen, and its market launch was delayed until September.[36] In that case, Amgen alleged that Sandoz did not make disclosures about patent information between the biosimilar applicant and the reference biologic maker that were required by law, and also alleged that Sandoz violated statutory notice requirements by providing notice of commercial marketing before Zarxio's approval. In the case's most recent disposition, a Federal Circuit sided with Sandoz and refused to grant an emergency motion for Amgen, effectively clearing Zarxio for market.[37]

V. STATE-LEVEL LEGISLATION

Key Issues

Each state regulates when and how a generic drug may be substituted for a brand-name prescription. However, concerns have been raised that these requirements may be misapplied for biologic drugs and biosimilars because a similar – though not identical – therapy may impact patients differently due to underlying variations in the medications themselves or manufacturing methods. The FDA has testified that a finding of interchangeability would have to precede any switching and then state law would govern substitution.[38]

Recognizing these questions, 31 states have considered legislation over the past two years that would set standards for substitution of a biosimilar product in place of the originator biologic.[39] Thirteen states have enacted such legislation. These laws usually require that any biosimilar product that is considered for substitution must first be deemed interchangeable by the FDA. Furthermore, because of the potential for one biologic to impact a patient differently than a competing biologic or biosimilar, many of the state biologic-related substitution statutes enable the prescriber to prevent a substitution by writing "dispense as written" or "brand medically necessary" on the prescription.

[36] Novartis press release, Sept. 3, 2015, available here.
[37] Amgen v. Sandoz, Appellate Decision, United States District Court for the Northern District of California, July 21, 2015, available here.
[38] Woodcock testimony, Sept. 17, 2015.
[39] NCSL website, available here.

In addition, many state rules for biologic substitution carry notice requirements to ensure that both the patient and the prescriber are notified if a substitution has been made by the pharmacy filling the prescription. In some cases, patient consent is required before the biologic drugs can be switched. Other common attributes of state biologic laws include recordkeeping requirements for substituted medications, online registries of approved interchangeable products, and pharmacist immunity from liability for substitutions made in compliance with state law.[40] Approximately 10 states have bills regulating biologic substitutions pending in their legislatures.[41]

Stakeholder Perspectives

Some stakeholders assert that this pending legislation, and already-enacted legislation like it, is premature and potentially overly restrictive because the FDA has yet to issue final standards for when a biosimilar is interchangeable. These stakeholders argue that state requirements may preempt patient access by restricting biosimilar availability before they even reach the market. Other stakeholders oppose the state legislation on the grounds that it is overly inclusive, citing concern that the laws could allow for a harmful substitution for a patient who is reliant on a specific biologic from a specific brand. Still other stakeholders support the legislation on the grounds that notice and recordkeeping requirements and other similar protections provide the transparency necessary to prevent a harmful substitution when the patient is reliant on a specific biologic strain. As biosimilars continue to be introduced, and more patients begin to rely on them, it is likely that more states will consider and ultimately enact substitution laws to help ensure that switching and substitution appropriately balance patient safety with potential cost savings.

VI. CONCLUSION

We hope this is a helpful overview of key issues relating to implementation of the BPCIA. We will continue to keep you apprised of further developments via real-time updates on regulatory releases and congressional action.

[40] *Ibid*.
[41] *Ibid*.