

## Research



# Reimbursement Policy for Biosimilars Will Have Negative Consequences for Patients

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## Introduction

The Centers for Medicare and Medicaid Services (CMS) have finalized a [rule](#) regarding the Medicare reimbursement methodology for biosimilar products. [Biosimilars](#) are prescription medications which have been approved by the Food and Drug Administration (FDA) as being “highly similar” to a specific biologic medication (known as the reference product).<sup>[1]</sup> Thus, it is easiest for most people to think of biosimilars as the equivalent of generics for small molecule brand name medications, though this is not scientifically accurate. While small molecule generics are chemically identical (save for potentially any inactive ingredients) to their respective brand name drugs—and can be because they are chemically manufactured—exact copies of biological products, by their nature of being developed from living organisms, cannot be produced,<sup>[2]</sup> and patients may respond differently to the reference product and the biosimilars.

In recognition that biosimilars are not simply generic versions of biologicals, the Biologics Price Competition and Innovation Act was included in the Affordable Care Act (ACA) to establish a different pathway for approval through the FDA and a different methodology for reimbursement from CMS. The law directs that biosimilars be paid based on 100 percent of their volume-weighted Average Sales Price (ASP) plus 6 percent of their reference product’s ASP. (For comparison, small molecule drugs are paid 106 percent of the volume-weighted ASP of all brand name *and* generic versions of a particular drug.) Biosimilars were given this more favorable add-on to the reimbursement rate in recognition that they are more expensive to produce than small molecule generics. However, there is now a debate as to whether or not biosimilars should be paid with a single billing code based on the ASP of all biosimilars for a single reference product, as has been finalized by CMS, or the ASP for each individual biosimilar, separately from any other biosimilar of the same reference product. Economic arguments and patient safety concerns may support the latter, though the statutory text regarding this matter is somewhat ambiguous.

## Biosimilars are Not Generics

There are several issues to consider when weighing these options. Biosimilars are not exactly the same as their reference biologic by definition. Biosimilars are also not required to treat all the same indications and conditions as the reference product. Therefore, one biosimilar may treat all or most of the same conditions as the reference product, while another biosimilar for that same reference product may only treat one indication. Further, even if two biosimilars of a single reference product treat the same indications, they are not necessarily biosimilar to each other (this would require a separate determination from the FDA). Thus, the biosimilar products are not necessarily equally effective or valuable and therefore should not be reimbursed the same amount. Reimbursing these drugs equally does not allow for fair compensation of higher quality products or the fact that one biosimilar may treat more indications than another, which presumably increases its cost of development. If price is the only factor on which companies are competing, a downward spiral may result, pushing prices to an

unsustainably low level, eventually forcing high-value manufacturers to exit the market. As competition is reduced, prices could eventually be allowed to rise for the few companies left standing, even if those products are not those most preferred by physicians and patients. The sterile injectable generic drug experience indicates that drug shortages can occur once the price has bottomed out.[3] The net effect of this policy, therefore, could be that the thriving biosimilars market that policy makers were expecting in the US might not materialize, and patients would not get the benefit of more treatment options and lower prices.

Further, because biosimilars will not be exactly the same, they cannot be used interchangeably (a drug must specifically receive “interchangeable” status by the FDA to qualify as an acceptable substitute without physician’s orders). However, some are worried that physicians may inappropriately prescribe such drugs interchangeably if the reimbursement amount is the same. This could happen either because the equal reimbursement inaccurately signals to the physician that the drugs are interchangeable, or because the price of a drug changes whereby a physician could lose money by prescribing one biosimilar which in turn encourages the physician to change the prescription. Conversely, physicians have the responsibility of ensuring they understand the differences between the drugs they prescribe, and drug manufacturers should take care to ensure this information is readily available.

## Difficulty Tracking Adverse Events

Another concern expressed by some is that using a single billing code will not allow for adequate pharmacovigilance to track and monitor adverse events among patients. If this is true, there is certainly reason to adjust this policy. Patients deserve to know that the biosimilars they are taking can be appropriately tracked to their respective manufacturer should there be a problem with a specific biosimilar.

Despite some claiming that the small molecule drug industry, which uses a single billing code (HCPCS), does not have problems tracking adverse events using the National Drug Code (NDC) assigned to each product along with the manufacturer lot number and company name for each batch of drugs produced, research by the Food and Drug Law Institute has found that adverse events for small molecule drugs are likely often misattributed to the innovator drug.[4] This happens because reports may only contain a nonproprietary name which results in drugs with the same nonproprietary name being grouped together.[5] Further, the FDA’s Adverse Event Reporting System (FAERS) database does not have a data field for an NDC number and the manufacturer lot number was only reported 10 percent of the time which would arguably make it difficult to rely on these pieces of information for tracking adverse events.[6]

Additionally, because biosimilars are not exactly the same as their reference product, as generics are for their brand-name drug, biosimilars may have a different clinical profile from the reference product and therefore potentially greater differences in the side effects, making the consequence of misattribution for biosimilars potentially much more severe. Finally, while biosimilars in the European Union, Canada, Australia, and Japan are all identified by the International Nonproprietary Name (INN) given by the World Health Organization (WHO), and those countries do not report problems tracking adverse events, WHO has stated that the current approach may not suffice as more biosimilars enter the market, at which point more distinct identifiers may be necessary.[7] In a report published by the National Center for Biotechnology Information, the authors state “the effectiveness of [current] surveillance methods may be compromised when there are multiple manufacturers of products that share common drug nomenclature or coding.”[8]

Some argue that the FDA naming practice, in which a unique suffix will be provided for each drug manufactured and added to the product’s proper name, will allow for sufficient pharmacovigilance. Others contend the FDA naming policy will not suffice, as a drug’s various naming and identifying components are not

always used in billing and the FDA's new Sentinel Initiative, to more effectively and accurately track adverse events electronically, will rely on multiple sources of information, including claims data.<sup>[9]</sup> The bottom line is the more differentiating factors, the better. The Secretary of Health and Human Services does not want to be in the position of finding out that the practice is insufficient *after* an adverse event occurs and the effected patients cannot be identified.

## The Statutory Text is Unclear

Finally, there is disagreement over interpretation of the statutory text which prescribes how biosimilars should be reimbursed by CMS. The reimbursement formula contains two parts: 100 percent of the ASP of the biosimilar product (the base payment) plus 6 percent of the ASP of the reference product (an add-on payment, typically provided, much like a dispensing and administrative fee). There is no disagreement over the part of the statute that states the 6 percent add-on should be calculated solely based on the volume-weighted ASP of the *reference* biological product, and that the ASP of the reference product should *not* be included in the base payment for biosimilar products, which is clearly and explicitly provided in §3139(a)(1)(B) of the ACA:<sup>[10][11]</sup>

Disagreement arises over CMS' reading of how to calculate the base payment. The text states that payment is the sum of:

“(A) the average sales price as determined using the methodology described under paragraph (6) applied to a biosimilar biological product for all National Drug Codes assigned to such product in the same manner as such paragraph is applied to drugs described in such paragraph; and

“(B) 6 percent of the amount determined under paragraph (4) for the reference biological product (as defined in subsection (c)(6)(I)).”;

CMS has interpreted this language to mean that all NDCs of all biosimilars with the same reference product should be combined to generate one shared ASP, just as all NDCs of small molecules (generic and brand name) are combined to create a single shared ASP. This position is supported by the explicit exemption of the reference product from the calculation of the base ASP, which is only necessitated if CMS's interpretation is correct, and by the ACA's reference to [paragraph \(6\)](#), which sets payment policy for multiple source drugs, as opposed to paragraph (4), which prescribes the payment amount for single source drugs or biologicals.

However, this same language is interpreted by others to mean that all NDCs of a single biosimilar product (each biosimilar may have multiple NDCs based on formulary variations, dosing, or other minor differences) should be combined to generate that product's unique ASP. They rely on the textual reference to NDCs of a single

“product”, and the financial differences between biosimilar and small molecule manufacturing (discussed *supra*) to support this position. If the latter interpretation is correct, biosimilar reimbursement would more closely resemble reimbursements for biologics than those for small molecule generics.

While Congress’ intent in using this particular language is unknown, in cases of statutory interpretation such as this, the administrative—in this case, CMS’—interpretation is accepted as correct.

## Conclusion

Ultimately, the decision over how biosimilars, or any medication, should be reimbursed by CMS should be determined by economic principles based on the value of the medication to patients and without putting patient safety and access to such products at risk. If the statutory text does not clearly provide for the favorable regulatory outcome of these factors, it should be amended. Because the rule finalized by CMS would provide equal reimbursement for all biosimilars of a single reference product, without regard for the relative value of such products based on factors such as the number of indications they are approved to treat or the side effects they cause, higher-value products may get squeezed out of the market. Even if CMS has appropriately interpreted the statute in development of this rule and in a consistent manner with how reimbursement policies have been determined for other drugs based on the same section of the law, the underlying policy appears to be flawed. This reimbursement methodology will likely lead to undesirable economic impacts, could stifle a fledgling biosimilars marketplace, and also lead to potential issues related to patient safety and access to appropriate treatment options, and therefore Congress should proactively fix this flawed approach.

[1] <http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm048341.htm>