ONCOLYTIC BIOSIMILARS: AN OPPORTUNITY TO REDUCE ONCOLOGY TREATMENT COSTS

EVERSANA™
ENGAGE

eversana.com

Richard Stefanacci, DO, MGH, MBA, AGSF, CMD, Chief Medical Officer, EVERSANA™ ENGAGE; **Craig Ornstein, PhD, MA,** Managing Director, Clinical Services EVERSANA™ ENGAGE; **Uttama Rath, PhD, MS,** Senior Medical Director, EVERSANA™ ENGAGE; **Jamey Hardesty, MPH,** Medical Strategist, EVERSANA™ ENGAGE; **Matthew Pakizegee,** PharmD, MS

Inclusion of oncology biosimilars in clinical pathways is one approach to reducing costs in this therapeutic area without compromising outcomes for cancer patients. There are currently eight Food and Drug Administration (FDA)-approved oncolytic biosimilars in the US market. Patients, providers, payers, policymakers, and manufacturers are all stakeholders that will be affected by these new biosimilars—and they all influence the placement of biosimilars in clinical pathways to ensure their appropriate use.

Several stakeholders within the healthcare system believe that drug costs are a major contributor to the rising total cost of care. However, this is not supported by the fact that only about 15% of healthcare spending is for prescription drugs.[1] Further complicating the matter is the fact that prescription drugs cannot be viewed in a silo; rather, they require assessment based on their impact on clinical and financial outcomes. Those who are attacking prescription drug costs—especially those for oncology treatments—need to look beyond inappropriate utilization restrictions that can negatively impact clinical and financial outcomes.

There are ways to reduce prescription drug costs without restricting utilization.[1] Oncology treatments have been an area of focus, as 80% of the most expensive therapies are biologics for cancer treatment.[2] From the payer perspective, oncology is a significant cost driver that can be contained through different tools, such as clinical pathways and oncology value assessments.[3] Inclusion of oncology biosimilars in clinical pathways is one approach to reducing costs in this therapeutic area without compromising outcomes for cancer patients. There are currently eight FDA-approved and marketed oncolytic biosimilars in the United States. Patients, providers, payers, policymakers, and manufacturers are all stakeholders that will be affected by these new biosimilars—and they all influence the placement of biosimilars in clinical pathways to ensure their appropriate use.

Biosimilars Market Implications for Stakeholders

The first oncolytic biosimilars have launched over the past year, and providers are starting to use them in the treatment of several types of cancer. The first three oncolytic reference products that have biosimilar competitors currently cost US commercial and government payers approximately $10 billion in peak annual sales.[4] Oncolytic biosimilars are clinically equivalent products that are highly similar but not identical to an approved reference drug, with no variations in efficacy, safety, and purity. Table 1 provides key terms and context required to understand the oncolytic biosimilar market. This is important so that stakeholders are speaking the same language as they discuss this relatively new area of opportunity.

Table 1. Key Terms and Context in Understanding Biosimilars

Biologic[8]	A diverse category of products; generally large, complex molecules that are extracted from or partially synthesized in living cells, such as a microorganism, plant cell, or animal cell, and are often more difficult to characterize than small-molecule drugs. For this reason, biologic copies coming from different cell lines are similar but not identical to the reference product. There are many types of biologic products approved for use by the FDA, including therapeutic proteins and monoclonal antibodies. Biologics are more expensive to produce than small molecules.
Small molecule[8]	Molecules usually composed of fewer than 100 atoms; they account for most FDA-approved products. Generic small-molecule compounds are bioequivalent and identical to the branded product. Manufacturing costs for a small molecule are relatively lower than those for a biologic. Generics are identical to their branded small-molecule counterparts.
Reference product[8]	The original biologic product, already approved by the FDA, against which a proposed biosimilar product is compared. Approval for a reference product is based on, among other things, a full complement of safety and effectiveness of the clinical trial data. A proposed biosimilar product is compared with and evaluated against this reference product to ensure no clinically meaningful differences exist between the two.
Biosimilar product[8]	A biologic product that is highly similar to, and has no clinically meaninful differences from, an existing FDA-approved reference product. Both biologic and reference products have a distinct brand name. A manufacturer developing a proposed biosimilar must demonstrate that its product is highly similar to the reference product by extensively analyzing (i.e., characterizing) the structure and function of both the reference product and the proposed biosimilar. Small differences in clinically inactive components between the reference product and the proposed biosimilar product are acceptible. Bioequivalence has to be demonstrated through pharmacokinetic and pharmacodynamic studies, an assessment of clinical immunogenicity, and, if needed, additional clinical studies.
Interchangeable biosimilar product[8]	The FDA has created this designation for an interchangeable product that is expected to produce the same clinical result as the reference product in any given patient. Additionally, for products administered to a patient more than once, further evaluation is required to assess the risk in terms of safety and reduced efficacy of switching between an interchangeable product and a reference product. No current biosimilar has been given this designation.
Substitution[8]	An interchangeable product may be substituted for the reference product without the involvement of the prescriber based on state laws. The FDA's high standards for an interchangeable designation should assure health care providers that they can have the same confidence in the safety and effectiveness of an interchangeable product as they would have for the reference product.
Immunogenicity[9]	A biologic's ability to trigger an immune reaction in the body upon administration, which may reduce the therapeutic effects of the biologic or even be life-threatening to the patient.
Oncolytic[10]	A biologic or small-molecule compound that destroys tumors.

Abbreviation: FDA, Food and Drug Administration.

Patients

From a patient perspective, oncolytic biosimilars are not currently on patients' radar, primarily because they have not been educated about biosimilars, and it is unclear who will inform them moving forward. A survey of 3198 patients revealed that almost 70% had never heard of biosimilars.[5] This knowledge gap among patients may be an issue if long-term outcomes show clinically significant differences between oncolytic reference products and biosimilars, because patients may not even know that they received a biosimilar. Although prescribers and pharmacists are required by most current state laws to disclose to a patient if the biologic product they are being treated with has been switched to a biosimilar by the pharmacy, if the prescription initially calls for a biosimilar, they may not be required to disclose this information.[6] It is important to note that all currently approved oncolytic biosimilars in the US are infusions that are administered by providers rather than patient-administered injections available at pharmacies. It is unclear the extent to which patients are receiving education from providers about the complexities surrounding biosimilars vs generic small molecules.

This discussion may even be more challenging if an oncology patient develops a distrust of a provider who prescribes a lower-cost biosimilar oncolytic product rather than its reference product. Many patients do their own research on the oncolytic therapies they are prescribed before or soon after they start taking the medication. Most of the information patients receive are from patient groups and manufacturers' product websites. They may discuss the prescribed biosimilar with their oncologist months after being started on it, and some patients may even ask to be switched to a reference product. In these discussions, it will be important to explain to patients that their out-of-pocket costs for biosimilars are expected to be lower compared with reference products because biosimilars have lower list prices.

Providers

The most important and influential stakeholders for oncolytic biosimilar acceptance and usage, oncologists and hematologists, have gaps in knowledge. Providers should be educated by their institutions and by manufacturers about biosimilar product issues such as immunogenicity, which may affect treatment outcomes, as well as the cost savings associated with these new products. Because biosimilars are generally manufactured using different cell lines than the reference product, there is concern that a biosimilar may produce antidrug antibodies, thereby impacting its efficacy or even rendering the reference product useless for a patient for subsequent therapies. Education around immunogenicity is needed to fully understand potential differences between reference products and biosimilars.

> **Oncolytic biosimilars have the potential to save the healthcare system billions of dollars each year as more biologics lose exclusivity.**

A survey of 376 oncologists found that 80% of them believed that it is important to be notified if a biosimilar is being substituted for the prescribed reference drug. Biosimilar substitution laws are determined by state, with many states requiring the physician to be notified if a substitution is made.[7] According to this survey, US oncologists were also more likely than their Latin

EVERSANA™

American or European peers to believe that patients could switch biologics from the reference product to a biosimilar mid-treatment and expect the same results. This is an important perception for clinical pathway developers, since making changes to a pathway may impact patients who have been on a reference product for months or even years.

One issue that will affect physician uptake of biosimilars is interchangeability, as it will have a major impact on pharmacists' ability to replace a prescribed reference product with a biosimilar of a generic product. To receive interchangeability designation, the manufacturer must demonstrate not only that the biosimilar has efficacy and safety equivalent to the biologic, but also that switching between the original biologic and the biosimilar is essentially equal to remaining on the reference product. The manufacturer has some advantages in having a certain degree of exclusivity; a subsequent interchangeable product cannot be approved for one year after approval of the first interchangeable biosimilar. The FDA has developed a clear pathway to interchangeability and is expected to designate the first interchangeable products within the next few years.

Payers

Payers may feel the need to find ways to incentivize physicians to prescribe biosimilars instead of biologics, as well as to provide patient education on cost and quality, to drive uptake. One approach would be to reward prescribers who adopt biosimilars more quickly. Another way is to prefer oncolytic biosimilars over reference products in terms of coverage and clinical pathways to reduce out-of-pocket spending when a biosimilar is prescribed or even by reducing the provider's administrative burden when a biosimilar is prescribed through no preauthorization. There are several risks to incentivizing a specific oncolytic biosimilar over a reference product, however, such as the potential for unexpected safety or efficacy issues or a lack of biosimilar supply due to manufacturing problems. Additionally, patient services provided by biosimilar manufacturers may not be on par with the reference manufacturer's patient services, creating a gap that leaves patients with higher out-of-pocket costs when a biosimilar is prescribed.

A better way to improve oncologist and hematologist trust in oncolytic biosimilars is to level the playing field with formulary policies that offer prescribers a choice between a reference product and its biosimilar, while requiring additional price concessions from the reference product's manufacturer to maintain parity coverage status.

Conclusion

Overall, oncolytic biosimilars have the potential to save the healthcare system billions of dollars each year as more biologics lose exclusivity. To ensure this cost savings, an educational campaign about these relatively new products must first be established to prepare for proper adoption by all relevant stakeholders, including employers. A foundation for this change can be clinical pathways that call out oncolytic biosimilars over their reference products as a means to promote this opportunity for cost savings.

Originally published in *The Journal of Clinical Pathways*, April 2020

EVERSANA™

REFERENCES

1. Yu NL, Atteberry P, Bach PB. Spending on prescription drugs in the US: where does all the money go? Health Affairs. July 31, 2018. Accessed March 24, 2020. https://www.healthaffairs.org/do/10.1377/hblog20180726.670593/full/

2. Lyman GH. Emerging opportunities and challenges of biosimilars in oncology practice. *J Oncol Pract*. 2017;13(suppl 9):7s-9s. doi:10.1200/JOP.2017.026831

3. Bender E. Cost of cancer drugs: something has to give. *Managed Care*. May 13, 2018. Accessed March 24, 2020. https://www.managedcaremag.com/archives/2018/5/cost-cancer-drugs-something-has-give

4. Sagonoswky E. Pfizer challenges Roche blockbusters with 3 biosim launches at discounts from 22% to 24%. January 24, 2020. Accessed March 24, 2020. https://www.fiercepharma.com/pharma/pfizer-challenges-roche-blockbusters-3-biosim-launches-at-discounts-from-22-to-24

5. Jacobs I, Singh E, Sewell KL, AL-Sabbagh, Shane LG. Patient attitudes and understanding about biosimilars: an international cross-sectional survey. *Patient Prefer Adherence*. 2016;10:937-948. doi:10.2147/PPA.S104891

6. Cauchi R. State laws and legislation related to biologic medications and substitution of biosimilars. National Conference of State Legislatures. Updated June 1, 2016. Accessed March 24, 2020. https://www.ncsl.org/documents/health/Biologics_BiosimilarsNCSLReport2015.pdf

7. Molinari A, Gewanter H, Reilly M, Kennedy B, Charles D. SAT0570 biologics and biosimilars: do physicians understand the differences? *Ann Rheumatic Dis*. 2016;75:875-876. doi:10.1136/annrheumdis-2016-eular.5829

8. Biosimilar and interchangeable products. US Food and Drug Administration. Updated October 23, 2017. Accessed March 24, 2020. https://www.fda.gov/drugs/biosimilars/biosimilar-and-interchangeable-products

9. Immunogenicity of protein-based therapeutics. US Food and Drug Administration. Updated March 27, 2018. Accessed March 24, 2020. https://www.fda.gov/vaccines-blood-biologics/biologics-research-projects/immunogenicity-protein-based-therapeutics

10. Oncolytic. *Collins English Dictionary*. Accessed March 24, 2020. https://www.collinsdictionary.com/us/dictionary/english/oncolytic