Healthcare system conversion to a biosimilar: Trials and tribulations

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Purpose. While biologic medications have transformed the care and management of millions of patients, they are a large financial strain on the healthcare system. Biosimilar medications present a great opportunity to improve care affordability. However, despite streamlined approval processes and the potential for cost savings, the acceptance and adoption of biosimilars have been slow. This descriptive report illustrates the preparation for, challenges of, and execution of an enterprise-wide biosimilar conversion within a large healthcare system. The 3 phases of biosimilar conversion utilized at our institution included selection of a biosimilar, pharmacy and therapeutics (P&T) committee approval, and implementation.

Summary. When selecting a biosimilar, clinical data, medication safety, cost, institutional cost savings, payer coverage, patient assistance programs, and additional patient services should be taken into consideration to ensure patient care is not affected. Understanding and endorsement of biosimilar use by physician leadership, care managers, and pharmacists are crucial before implementation. P&T committee approval with clear delineation of the patient population (naive vs experienced), disease states, and whether the biosimilar would be the preferred medication should be obtained. Transparent communication of clear expectations to patients and coordination with the information technology (IT), contracting, and supply chain departments are necessary before the go-live date. Contracting and IT implementations should ideally take potential changes in biosimilar adoption into consideration and have enough flexibility to account for these changes. Planned evaluations of patients' experiences with the change to the biosimilar should be incorporated as part of the implementation plan.

Conclusion. The barriers to biosimilar adoption are plentiful. Careful planning, clear communication, and coordination with all affected disciplines can ensure successful biosimilar conversion.

Keywords: biological products, biosimilar pharmaceuticals, formulary, pharmacy and theraputics committee

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The pharmaceutical industry and healthcare system have been revolutionized by the development of biologic medications. These medications have transformed treatment guidelines for numerous health conditions, improved patient quality of life, and could potentially alter the course of a disease.[1,2] However, they are also associated with increased cost of care. While biologics may be cost-effective through the generation of value via improved patient care, they still represent a financial constraint for the healthcare system. Although biologic medications correspond to about 2% of all prescriptions in the United States, they make up 37% of total medication spending.[3] Furthermore, since 2014, 93% of overall growth in prescription medication costs can be attributed to biologic medications.[3]

Biologic medications are more structurally complex than small molecule medications, with more intricate

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manufacturing processes and requirements for storage and handling. While small molecule medications are manufactured through chemical synthesis, biologics rely on the use of living systems.[4] Hence, it is not possible to develop an exact, chemically identical copy of a biologic agent. In fact, even serial batches of referenced biologic medications have some level of variability.[5] As reference biologics reach the end of their patent cycle, biosimilar medications present a great opportunity to improve care affordability. It was estimated that referenced biologic medications corresponding to about $30 billion in sales in the United States would lose their patent protection by 2020.[6] Given the differences in manufacturing processes, the traditional Food and Drug Administration (FDA) approval process for generic medications does not apply for biologic medications. However, the Affordable Care Act created a more efficient licensing and approval pathway for biosimilars. FDA defines a biosimilar as "a biological product that is highly similar to and has no clinically meaningful differences from an existing FDA-approved reference product."[7]

Despite streamlined approval processes and the potential for dramatic savings, the acceptance and adoption of biosimilars have been slow. By the end of 2019, only 11 of the 26 biosimilars approved by FDA were actually marketed.[8] Furthermore, even approved biosimilars have difficulty garnering patient and physician acceptance. As of 2018, less than 1% of biologic volume was captured by biosimilars.[9] The reason for this slow response to biosimilar market penetration is multifactorial, including a lack of clinician awareness, patient reluctance, local hospital or payer formulary restrictions, and the complex and siloed medical health system in the United States, among other factors. Furthermore, although biosimilars are less expensive than their referenced counterparts, there is usually only about a 15% discount when only 1 biosimilar is available.[10] It is possible that the marginal decrease in cost may partially account for the lack of uptake. Recognizing the challenges associated with the implementation of biosimilars, national societies have published guidance documents on their use.[11-14] Specific to the formulary management of a healthcare system, these guidance documents all stress the importance of provider and patient education. In addition, the guideline from the National Comprehensive Cancer Network (NCCN) recommends that biosimilars undergo similar pharmacy and therapeutics (P&T) committee review as new branded medications.[11] This recommended method is different from the usual approach for generic small molecule medications.

Conversion from referenced infliximab (Remicade; Janssen Biotech, Horsham, PA) to infliximab-abda (Renflexis; Samsung Bioepis, Yeonsu-gu, Republic of Korea) was recently implemented at the Cleveland Clinic Health System (CCHS). This conversion was widespread, with mandatory adoption across all medical disciplines. The conversion required considerable planning, education, execution, and collaboration from many different departments within the institution. This review highlights the process taken to ensure successful biosimilar conversion. Key points from each phase of implementation can be found in Table 1.

KEY POINTS

- Selection of a preferred biosimilar product requires a balance of clinical data assessment, contracting negotiations, analysis of cost savings, and examination of the availability of patient assistance programs.
- Institutional conversion to a biosimilar requires careful planning, prescriber buy-in, and coordination between multiple clinical and supportive departments.
- Transparent communication of expectations and education to both patients and prescribers will help facilitate successful biosimilar conversion.

Biosimilar implementation process

Selecting a biosimilar. Significant effort was devoted to selecting a biosimilar for infliximab at CCHS. At the time of selection, there were 2 biosimilars approved by FDA (infliximab-abda and infliximab-dyyb). The 4 components evaluated to inform final biosimilar selection included available clinical data, cost, manufacturer programs (eg, patient assistance, free medication, and other patient and provider hub services such as education and monitoring), and commercial and government payer coverage. Unlike small molecule generic medications, whose FDA approval relies on demonstration of bioequivalence, the approval process for biosimilars involves demonstration of comparable safety and efficacy. This provides a unique opportunity to evaluate treatment outcome data in which the biosimilar is directly compared with the referenced medication. Evaluation of clinical data, including the studied populations and findings, to determine whether the evaluated biosimilar would have comparable effects on the intended population at the local site is an important step in selecting a biosimilar. Additionally, if there are switch studies, these help add to the review of clinical data for patient outcomes, including any issues with immunogenicity. There were switch studies available at the time CCHS reviewed the infliximab biosimilars.[15-20]

One of the major incentives for conversion from a referenced medication to a biosimilar is the cost savings. Hence, evaluation of cost and pricing is a crucial step in selecting a biosimilar. At CCHS, the selection of a biosimilar for infliximab was purposely delayed

until there was more than 1 biosimilar on the market. This course of action was chosen because the cost of any biosimilar (or referenced medication) drops more substantially when there are more than 2 manufacturers available. The clinical data and potential cost savings associated with each biosimilar should be considered simultaneously. Engagement with institutional contracting and purchasing departments should also begin at this stage to initiate negotiations with the manufacturers to obtain the best pricing information. While cost evaluations are important for local institutional finances, similar evaluations should be undertaken to ensure the cost and level of service for patients will not be affected by a switch to a biosimilar.

The level of service provided by the manufacturer in terms of patient assistance programs, copay supplements, and educational programs should be evaluated to ensure that a level of care similar to that with the referenced medication can be maintained. For example, during this process at CCHS, it was discovered that the patient assistance programs for 1 of the biosimilars would not be available to patients who were using infliximab for an off-label purpose. This preliminary evaluation prevented patients who might have financial needs from being converted to a biosimilar they might not be able to afford. Efforts were also devoted to assessing the current payer mix among patients using infliximab to ensure that the selected biosimilar would have similar insurance coverage. In addition to an evaluation of the payer mix and level of service, a history of medication supply issues was ascertained to minimize the possibility of detrimental interruptions associated with potential medication shortages. After careful consideration of local institutional and patient needs, infliximab-abda was selected as the biosimilar for infliximab at CCHS.

P&T committee approval. While the P&T committees at most health systems do not oversee generic substitutions,[21] the P&T committee at CCHS elected to consider biosimilars as a new formulary request. Because P&T committee approval was required at CCHS, which necessitated a physician request, this provided an opportunity to engage physician leaders from different disciplines who might be affected by the conversion of infliximab to a biosimilar. Each institution should have an open discussion regarding whether biosimilars should be considered a generic substitution or a new formulary request review. Regardless of the requirement for P&T committee review, the opportunity to present a biosimilar to the committee may garner more physician engagement and support, which may ultimately lead to an easier transition.

P&T committee discussions should also entail considerations of the preferred medication if approved, patient populations that might be excluded from conversion, and whether conversion should be limited to naive patients only. These discussions at CCHS led to the decision that infliximab-abda was to be the preferred medication for both naive and experienced patients throughout the institution for inpatient use. It was also decided that it would be the preferred agent for outpatient use, unless a patient's insurance plan would not cover the medication. Pediatric patients were excluded from this conversion because of a lack of support from CCHS Children's Hospital providers. These providers wanted to defer conversion to first see the experience and outcomes of use in the CCHS adult patient population. These decisions were made at CCHS because clinicians agreed that having a biosimilar as a preferred medication was more likely to ensure increased usage and conversion of both naive and experienced patients would minimize confusion and potential errors. Lastly, a preferred biosimilar may also be advantageous for contract negotiation purposes if the manufacturer can be assured of a certain market share.

Approval to implementation. At CCHS, over 6 months transpired between the P&T committee approval date and the actual date for institutional conversion. During this period, an immense amount of work was done to ensure a successful transition to infliximab-abda, which included physician education and communication, information technology (IT) involvement, payer and manufacturer negotiations, inventory management, and patient communication. The manufacturer of infliximab-abda was instructed to provide a single point of contact where all internal questions from pharmacy, nurses, and case managers could be directed.

Given their long, cultivated relationships with patients and difficulties in disease management, it is reasonable that there is some apprehension among physicians about switching to a biosimilar. As such, institutional biosimilar implementation cannot be solely driven by pharmacy departments. While pharmacists can prepare and provide educational material, strong physician leadership and institutional support are crucial in ensuring compliance with new standards. At CCHS, engagement and education of physicians started with the chair of each clinical department that was going to be affected by the biosimilar conversion. Education was also provided to each prescriber to ensure that all aspects of ordering and preauthorization were understood. This also allowed for the incorporation of feedback from frontline physicians.

The IT department played a significant role in the conversion from infliximab to a biosimilar at CCHS. Their involvement included identifying treatment-experienced patients, editing existing prescription records for all treatment plans to default to infliximab-abda, and extracting patient insurance information. The initial data query for patients receiving infliximab included patient demographics, insurance, treatment location, and treatment plan information. Because it was decided that treatment-experienced patients would be included in the conversion, it was imperative to identify these patients so that their prescription orders could be

manually converted to the biosimilar in the electronic health record (EHR). The list of these patients was also important as it allowed coordination of the pharmacist workflow before the switch date and provided insurance information to prior authorization departments to facilitate insurance approval. Through this process, it was determined that approximately one-third of the patients currently receiving infliximab could not be switched to infliximab-abda owing to insurance coverage reasons. Infliximab was part of many treatment order sets, and IT was also instrumental in ensuring that all order sets were updated to preferentially select infliximab-abda. For patients who were not eligible for the conversion, it was important to make sure that the referenced medication was still available to be ordered. Because patients' insurance information and insurance coverage for biosimilars are dynamic, provisions should be included in prescription file builds to increase flexibility and accessibility for future changes. For example, although not available at the time of CCHS conversion, prescription files with orderable mapping may allow for the EHR system to dynamically select the infliximab product that corresponds with a patient's insurance coverage. Lastly, IT involvement identified where infliximab was being given most frequently. This volume information was helpful to facilitate inventory management so that no sites were left without adequate medication supply after implementation. Altogether, the IT department converted 50 treatment order sets, taking about 40 hours of programming time.

Supply chain and contracting departments were equally important in biosimilar implementation. Contract negotiations should entail trying to obtain the best pricing for the institution while maintaining a high level of flexibility based on market fluctuations. For example, because payers' preferential coverage for infliximab or one of the biosimilars may change over time, it is crucial to have escape clauses included in the contract that take these factors into consideration. Furthermore, as more biosimilars for infliximab are likely to become available, there should also be provisions to ensure that contract prices remain competitive with market value. Supply chain and contracting departments also frequently have communication with institutional departments that handle market access. Leveraging the relationship with market access departments for communication with payers may help inform them of changes made at the hospital. With enough hospitals changing to biosimilars, this might provide an impetus for payers to provide coverage for more biosimilars.

Patients should continue to be at the center of all treatment-related decisions. As such, transparent communications describing the change to infliximab-abda were sent to all treatment-experienced patients 2 months before the conversion date. The letter was targeted all patients who received at least 1 dose of infliximab in the previous year. It described the biosimilar conversion and also provided information regarding patient assistance programs with the biosimilar. In addition, contact information for the institutional drug information center was provided, in the event that patients had further concerns.

The steps taken by CCHS in the implementation of infliximab-abda mirror many of the recommendations from the recent NCCN white paper on the safe and efficient use of biosimilars.[22] In particular, use of the P&T committee to determine the preferred biosimilar, leveraging the EHR to drive practice change, and

Table 1. Key Points and Lessons From Each Phase of Biosimilar Adoption

Phase	Key Points
Selecting a biosimilar	• Consider clinical data, cost, payer coverage, and patient assistance programs • Consider delaying selection until more than 1 biosimilar is available • Ensure patient services will not be affected by switching to a biosimilar
P&T committee approval	• Obtain clarity regarding whether biosimilars are considered new formulary requests or generic substitutions • Engage physician leaders in the process of obtaining approval • Determine whether implementation of a biosimilar would be for treatment-naive patients only or also for treatment-experienced patients • Determine whether the referenced product or biosimilar would be the preferred product • Decide whether any specific population or disease state will be excluded from the biosimilar conversion
Implementation	• Transparent communication about conversion with patients and physicians • Engage with the IT department to update order sets and identify treatment-experienced patients (if applicable) • Finalize contracting and supply chain, ensuring adequate supply, favorable pricing, and flexibility for future developments • Plan for future evaluations of biosimilar adoption and patient response

Abbreviations: IT, information technology; P&T, pharmacy and therapeutics.

preliminary work to understand the payer landscape to minimize interruptions in care were discussed in the white paper.

Implementation to evaluation. Adoption of biosimilars in the United States has been slow.[23] The conversion at CCHS provided a unique opportunity to evaluate the real-world experiences of patients in switching to a biosimilar. Furthermore, owing to differences in payer coverage, it also provided an ideal natural experiment for multiple comparisons. These included treatment-experienced patients compared to themselves after the conversion to infliximab-abda, novel patients started on infliximab vs those started on a biosimilar, and treatment-experienced patients continued on infliximab vs those who were switched to the biosimilar. Institutional adoption of the biosimilar across multiple medical disciplines also allowed for comparison of patient responses across different disease states. Given the paucity of real-world data on biosimilar conversion in the United States, it is imperative that institutions converting to a biosimilar be proactive in identifying opportunities for systematic evaluation. These data may help further accelerate conversion to biosimilars in the United States. At CCHS, evaluation of all these potential comparisons is currently underway.

Conclusion

Implementation of a new biosimilar at a large medical center requires careful planning, transparency, provider and patient affirmation, and collaboration between contracting, purchasing, and IT departments. The experience from the infliximab-abda implementation process will be used to inform future biosimilar conversions for rituximab, bevacizumab, and trastuzumab at CCHS.

Disclosures

The authors have declared no potential conflicts of interest.

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