Per the United States Food and Drug Administration (FDA), a biosimilar is “a biological product that is highly similar to a US-licensed reference biological product for which there are no clinically meaningful differences in safety, purity, or potency of the product.”\(^1\) Despite minor differences in clinically inactive ingredients, biosimilars are approved by the FDA to be highly similar to reference biological products in terms of safety and efficacy. As such, their introduction into the treatment landscape provides more therapeutic options, which ultimately may lead to greater affordability for patients. Biosimilars in oncology have been shown to be efficacious in both supportive and therapeutic care, and health care organizations in the United States have started incorporating them into treatment management for patients.

One large health care organization embracing biosimilars is M Health Fairview, a partnership between University of Minnesota, University of Minnesota Physicians and Fairview Health Services, an integrated health system. Headquartered in Minnesota and serving the entire Greater Minneapolis-St Paul metro areas, as well as communities throughout greater Minnesota, portions of northern Iowa, and western Wisconsin, M Health Fairview combines the University’s deep history of clinical innovation and training with Fairview’s broad continuum of health care services. This includes hospitals, primary and specialty care clinics, retail and specialty pharmacies, as well as pharmacy benefit management services, rehabilitation centers, counseling and home health care programs, and numerous other services.\(^2\)

The mission of the Cancer Care Service Line at M Health Fairview is to provide consistent academic-level cancer care to all patients throughout their entire health system. Their model is designed to treat the whole system as if it were a single clinical service entity, utilizing system resources to ensure access to care for patients. M Health Fairview employs more than 50 medical oncologists and has 10 infusion centers, 4 of which are dedicated to cancer care. Home infusion services are a strong focus for the organization.

Although M Health Fairview has experience in the use of biosimilar products in non-oncology areas and supportive care in oncology, this report, or “road map,” documents efforts associated with the uptake of therapeutic biosimilars by the Cancer Care Service Line. Key stakeholders from M Health Fairview who were interviewed and provided insights to generate this road map included the oncology service line chief, oncology pharmacy program manager, chair of the cancer care quality committee, and clinic operations director.
Oncology-Centric Biosimilar Implementation at M Health Fairview: 
A Review of Process and Perspective

Key Learnings

After 6 to 9 months of initial planning, M Health Fairview implemented the adoption of therapeutic biosimilars in December 2019. Once their safety and effectiveness had been established, the driving factor for use of biosimilars was financial and, in part, driven by insurer directives and coverage policies.

Although M Health Fairview did not set out to be the first health system to develop an organized approach to biosimilar implementation, there was a desire to take a proactive stance on biosimilar use ahead of insurer mandates. Previous experience with supportive care biosimilars, both within the Cancer Care Service Line and outside the service line in other therapeutic areas through pharmacy services, aided in this decision.

Highlights of M Health Fairview’s key learnings and processes are noted here and detailed below:

Clinical Leadership and Decision-Making

In health system–sized organizations, multiple layers of stakeholders can affect biosimilar product uptake and utilization. Input and buy-in from various levels are necessary for successful implementation.

Although there are few formulary limitations for oncology treatments because of the diversity of products, more guidance will be needed for biosimilars that have nearly the same therapeutic function. This includes consideration of clinical data as well as practical product characteristics.

Operational Integration of Biosimilars

Implementation of biosimilar adoption should be operationalized in an electronic medical record (EMR) or other platform to enable an easy and seamless experience for physicians that also respects prescribing regulations.

An inherent and strong trust between medical service providers (eg, physicians and nurses) and pharmacy services is a strong enabler for successful uptake of drug utilization policies and programs.

Biosimilar Education

Stepwise approaches to education are useful for developing foundational and core understanding of biosimilars and should be followed by practical product-specific information for health care providers. Once applied, regular reinforcement is valuable to ensure uptake of core concepts as more biosimilar products become available.

A strong and consistent educational platform for health care providers will ensure a strong and consistent approach to patient education.
Clinical Leadership and Decision-Making

At M Health Fairview, several committees exist within the Cancer Care Service Line that provide structure and leadership. These include a lead cancer committee, a cancer care quality committee, site-specific leadership committees, therapeutic specialty committees, and the formulary committee.

The lead cancer committee is responsible for setting overall goals and direction for the service line, whereas the cancer care quality committee is focused on consistency of care aligned with quality metrics.

Decision support for practitioners is managed through protocols directed by therapeutic specialty committees aligned by cancer type (eg, breast, lung, colorectal, hematological). Each committee meets monthly and reviews any changes or change requests before their implementation. These can include changes to order sets for new or updated treatment options as well as updates to care plans or other protocols requested by physicians.

Formulary Management at M Health Fairview

The formulary at M Health Fairview is utilized by all hospitals and clinics within the network and is maintained by a Pharmacy & Therapeutics (P&T) committee. Updates to the formulary are guided by specialized therapeutic subcommittees which are responsible for analysis of clinical and economic data, documentation in the form of detailed drug monographs, and generation and presentation of formal recommendations to the P&T committee. A system-level oncology formulary subcommittee is responsible for the management of available medical oncology therapeutics. This interdisciplinary subcommittee is led by an oncology pharmacist and includes several leaders from the physician and advanced practice nurse teams.

Biosimilar Considerations

“We evaluate biosimilars based on safety and efficacy first, as patients are our first consideration. The process of FDA review and approval of biosimilars provides us with trust that these products are safe and effective.”

– Oncology Pharmacy Program Manager at M Health Fairview

The oncology formulary is based generally on National Comprehensive Cancer Network (NCCN) guidelines, wherein use of specific biosimilar products is not stipulated. Therefore, the formulary subcommittee carefully evaluates available products for practical management based on available clinical data and practical product characteristics.

Before therapeutic biosimilars were brought to the formulary subcommittee, products were reviewed by several provider champions and key physicians who were caring for those patients with the respective indication(s); acceptance of the biosimilar onto the formulary by the subcommittee was obtained quickly upon review of the product data gleaned from these reviews.

Evaluation of biosimilars (regardless of supportive care or therapeutic use) started with a review of clinical data: patient safety is paramount in this process and a priority, followed by efficacy. After that, financial considerations were considered. Also, part of the goal for a thoughtful and practical approach to biosimilar adoption was consideration of insurer-directed coverage policies so that access and availability aligned with major insurers in the region.
Differentiation of Biosimilar Products

In addition to key clinical factors and financial considerations, differentiation of biosimilar products between reference and other biosimilars can include more subtle attributes and characteristic, as follows.

- **Packaging.** As a practical matter, how products are supplied can affect their use and be a competitive differentiator. For example, Herceptin (trastuzumab) is only available as a 150-mg single-dose vial, which the formulary subcommittee at M Health Fairview determined can lead to wastage. An evaluation of competing biosimilars revealed that a multidose vial was available and was deemed less wasteful.

- **Logistics/availability.** Contracting with manufacturers with a proven track record of accurate, on-time shipment fulfillment is important. An early experience with an immunoglobulin shortage taught M Health Fairview that a manufacturer’s ability to offer products more consistently can have a substantial impact on practice.

- **Patient support.** Patient assistance and support programs offered by manufacturers are valued and were found to be potential differentiators among products with comparable clinical attributes.

Operational Integration of Biosimilars

Once a product has been approved for use in a protocol, it must be integrated into the EMR. Physicians can document cancer staging and manage chemotherapy through the EMR by creating and personalizing treatment plans based on standard oncology protocols. At M Health Fairview, these protocols are created, vetted, and approved by the practice committees. Once protocols are approved, operationalization can occur within days of development.

When the M Health Fairview team considered bringing biosimilars into the EMR, it became clear that the system not only needed to be easy for the physicians to use, but also developed to allow for back-end implementation of updates in a way that would not interrupt their practice activities.

An additional consideration specific to M Health Fairview was that in Minnesota, substitution of a biosimilar product is considered a prescription change and therefore requires a physician order.

The solution M Health Fairview introduced to streamline biosimilar integration had 2 major components:

1. **Brand-agnostic representation.** Biosimilar therapy options are presented as the core molecule with a “starred” 4-character suffix (eg, bevacizumab-****) instead of the biosimilar suffix assigned to unique products (eg, bevacizumab-awwb), thereby recognizing the therapeutic agent (or molecule) but not the manufacturer. Physicians have the ability to override this; however, to do so, a series of deliberate and specific steps within the system are required.

   - Programming of the system allows potential substitution of different biosimilar products without adjustment of the user interface and potentially confusing the physician.

2. **Policy development.** Given the state regulations requiring physician orders for substitution of biosimilars, a substitution policy agreement within the health system was developed and approved by practitioners. This enables pharmacy services to actively select and dispense biosimilar products without repeated requests to the physician at the time of dispensing to update or re-enter the order.

   - Success of this effort, noted by multiple stakeholders, is due to the strong sense of trust, high level of service, and collaboration with pharmacy services.

   - Additionally, due to regulations, the actual product that is dispensed is noted and recorded in the EMR and patient record and shared with the prescribing physician.

   - Also of note, although verbal consent is needed from patients before starting chemotherapy, patient consent is not required for use or substitution of a biosimilar product.
Logistics and Administration
At M Health Fairview, orders for infused [oncology] therapies are typically placed 2 to 3 days before the desired time of administration. A financial team reviews the order for eligibility by an insurer or other third-party payer and may request adjustment of the product selected (eg, from a reference product to a biosimilar, from a biosimilar to another biosimilar, or from a biosimilar to a reference product) based on insurer requirements.

After adjudication by the financial team, orders are then sent to the respective infusion center. Pharmacy services are embedded in each location to support dispensing of the product. Each location typically stocks 7- to 10-day supplies of both reference and biosimilar products. Multiple wholesalers are utilized for fulfillment based on supply needs and potential seasonal logistic challenges (eg, Minnesota winters).

Once a biosimilar is dispensed from the pharmacy, onsite nursing staff at the infusion center are responsible for administration of the product, as well as patient education. (Of note: in home infusion settings, a different level of health care professional [eg, medical assistants] may be responsible for product administration.)

Biosimilar Education

“The initial level of understanding about biosimilars was notably varied among stakeholders, with some practitioners having a good understanding of biosimilars and others hearing about the products for the first time as they were being rolled out at M Health Fairview. Education of staff became a priority because that enabled information to flow to patients.

Biosimilar education for the staff was prepared and delivered by a pharmacy services team and followed a phased approach, starting with the concept of biosimilars, followed by product-specific information and organizational policies, such as the aforementioned biosimilar substitution effort.

Physician Education
Physician thought leaders within a department or disease team were approached first to discuss specific informational needs. This was followed by presentations to larger groups. Initial educational efforts focused on the regulatory pathway for biosimilars and were then followed by product-specific clinical data relative to the reference product to address educational gaps.

Outside of live presentations, information such as policy and procedure updates were typically delivered through email communications. The service line’s newsletter also functioned to reinforcement general biosimilar information as well as biosimilar-specific topics.

It was noted that the easiest method for understanding biosimilars was to explain their relationship to the reference product as analogous to generic and brand name small-molecule drugs. Although another commonly used analogy involved immune globulin, whereby the products have close or identical indications but different sources and even varying formulations, the “generic drug” analogy was particularly useful when discussing biosimilars with patients.

Overall, M Health Fairview physicians were described as being very comfortable with biosimilar adoption and the policies associated with their use, and active communication among teams has resolved any concerns.

Nursing Education
Because patient education is a responsibility of the infusion center nursing staff, pharmacy services spent additional time on training these teams. Training sessions were held during staff meetings that included...
nurses, nursing managers, and other team members. Pharmacists supporting each infusion center helped to reinforce key concepts.

Product-specific information related to drug administration and patient monitoring was a significant training focus for this group, in addition to general background and conceptual information about biosimilars. Drug product and policy documentation for biosimilars is distributed in the same manner as that for any other drug or therapy in the service line.

An additional distinction in training for nursing staff was the specific recognition of the product itself, including the bags and labels that are visible to patients. This further prepared staff to ensure the appropriate product was dispensed and provided an opportunity to communicate with patients on the biosimilar as needed.

**Education Improvements**

Although all stakeholders noted that sufficient information was provided to staff to allow effective uptake of biosimilars at M Health Fairview, there were some challenges and potential areas for improvement, as follows.

- **Interdisciplinary training.** Based on identified practical needs, physicians and nurses have been offered different and separate biosimilar education—that for physicians focusing on product selection and therapeutics, and that for nursing staff focused on administration and monitoring. Although this was useful, there were suggestions that decompartmentalizing educational programs might provide broader insights to all involved.

- **Earlier education.** For nursing staff in particular, an earlier and longer learning cycle could help support retention of information that could pass on to patients. These efforts could also include peer-based education and organized reviews of externally supplied information.

- **Other provider education.** For home infusion services, a different level of health care professional (eg, medical assistants) was described as providing administration services. Because these team members also are patient-facing, consideration should be made for their education to ensure consistent patient messaging.

**Patient Education**

Nurses in the infusion centers at M Health Fairview are responsible for patient education during chemotherapy and administration of other infused drugs, including biosimilars. Pharmacists provide education for patients who receive oral oncolytics and they also support the nursing staff for all patient education needs.

The level of health literacy among patients in the infusion center can vary substantially. Some patients do not understand their treatment options, even at the time of infusion, whereas others are very engaged and aware of everything that is occurring in the infusion chair.

Patient education on biosimilars often includes the following key points:

- Acknowledgment that the product being administered to them is a “biosimilar” and what that means. It was noted that patients are commonly aware of infusion bag labels (and other packaging) and will start their questioning after noticing label differences.
- An understanding of a patient’s potential perception of a biosimilar and anticipation of potential questions and concerns (eg, “Does it work?”, “Is it safe?”, “Why is this product being used?”, “Is my doctor aware of the product being used?”).
- Reinforcement on efficacy and safety of biosimilar products to ensure there is confidence in the treatment.

Because of the difficulty in managing printed patient education materials, an online vendor was used to produce and deliver a variety of content in which treatments were identified by generic or molecular names rather than brand names.

**Results: Successful Implementation of Biosimilars**

“We consider the adoption of the therapeutic biosimilars in oncology a success. In fact, implementation was much easier than I had anticipated. I think the comfort in the process and teams that supported the entire effort, from education to operationalization, brought it together.”

– Oncology Service Line Chief at M Health Fairview
The strategies and processes described herein helped drive the successful implementation of therapeutic oncology biosimilars at M Health Fairview. The Figure (provided by M Health Fairview) shows the transition from the use of reference products for bevacizumab and trastuzumab to biosimilar versions beginning in December 2019 through April 2021. Over the course of this period, the use of biosimilar products went from nearly zero to comprising 76% of all bevacizumab administrations and 78% of all trastuzumab administrations at M Health Fairview.

Conclusions
Although there were notable clinical and operational needs identified with the uptake of biosimilars, the implementation effort was described by M Health Fairview providers as “easier than I thought it would be.” The process for inclusion in practice was smooth, and provider and patient attitudes and acceptance of biosimilar products were seemingly based on the strong presence of and confidence in pharmacy services across stakeholders. This strong presence also provided a great deal of trust in the development and implementation of policies related to biosimilars within the Cancer Care Service Line. The planning and execution of these policies were likely fed by the pharmacy services’ substantial experience in formulary management and drug utilization across the large health system.

The focus by pharmacy services in developing a strategy that was practical, seamless, and easy for physicians to follow was a hallmark of the plan at M Health Fairview. The education and continual support and reinforcement by pharmacy services and pharmacists at all levels in the organization continue to drive the process and further adoption of biosimilars.

References