

NCCN Pharmacy Directors Forum Recommendations on Operationalizing the Safe and Efficient Use of Biosimilars in the Clinical Setting

Abstract:

Biosimilar medications have the potential to reduce expenses to our overall healthcare system, and their adoption by payors and providers is starting to significantly increase. However, adopting these medications into a clinical setting is impacted by external as well as internal forces which create unique challenges. A working group within the Pharmacy Directors Forum of the National Comprehensive Cancer Network (NCCN) has reviewed and highlighted some of the potential challenges regarding adopting biosimilars into clinical practice. The work group has summarized several recommendations for the safe and efficient use of biosimilar medications in the clinical setting.

Executive Summary:

Although biosimilar medications have the potential to lower healthcare costs, there are significant challenges from an operational standpoint and unique risks that exist when using these products in the care of patients. These risks include medication errors, financial toxicity for patients, and economic challenges for institutions/providers. Payor policies, such as single sourcing coverage of biosimilar medications, can be a root cause of some of these risks. A robust process around the operationalization of biosimilars can help mitigate some of this risk. The National Comprehensive Cancer Network (NCCN) Pharmacy Directors Forum – Biosimilars Work Group created a survey for the entire NCCN Pharmacy Directors Forum network to understand some of the most significant risk points. Based on the results of this survey, several areas were identified that should be addressed when introducing a biosimilar in a hospital and/or hospital-based infusion center. These focus areas should include assessment of patient safety, vigilance to payor policies including restrictions to specific products, leveraging the electronic health record (EHR), thoughtfulness with the storage of multiple biosimilar products, and close coordination with revenue cycle/finance. The NCCN Pharmacy Directors

Forum – Biosimilars Work Group assigned content experts from the work group to lead each risk point.

Input from all the work group members was utilized to create this position paper on operationalizing the use of biosimilars for health systems/cancer centers.

Overview and Background:

Biological drugs created through recombinant DNA technology have played an extremely important role in the treatment of numerous malignancies revolutionizing the treatment landscape. These medications are large molecules derived from living sources that are highly complex to produce. Variability exists between different biosimilar manufacturers and the reference product. In fact, there can be intra-lot variability between lots or batches by the same manufacturer, including the reference product.¹ Therefore, biosimilar medications are not generically equivalent and are not exactly identical in every way to the reference product. However, they are highly similar to, and have no clinically meaningful differences, from an FDA approved reference product.

The path for biosimilar products to gain FDA approval through an abbreviated pathway was created by the Biologics Price Competition and Innovation (BPCI) Act of 2009. The primary goal of the BPCI Act of 2009 was to reduce the cost of biologic therapies and increase access to safe and effective biological products. Sponsors can submit a Biologics License Application (BLA) which is incorporated into section 351(a) of the Public Health Service Act. Through this abbreviated pathway, drug development expenses are lessened. Biosimilar products are a model solution to reduce total expenditures in the biologic product market by as much as \$150 billion by some estimates.² Biosimilars typically receive the same FDA indications as the reference product except for regulatory protected indications – for example, the orphan status indication for bevacizumab (Avastin® – Genentech) in ovarian/gynecological cancer. The FDA generally will require clinical trials in some of the indications with outcomes that include response rates, mortality, and/or safety monitoring. Although the BPCI Act allows for interchangeability of biosimilar medications, none of the commercially available biosimilar

products are considered interchangeable as of the date of this document. The Purple Book has a listing of biological products and indicates whether they are interchangeable with a reference product.³ Therefore, except under certain conditions, such as authorized interchange by medical staff, changing between one manufacturer's medication and another's cannot be done automatically without permission of the provider that wrote the original order. Hospital policies and procedures congruent with state regulations should be created and followed for each institution. The National Conference of State Legislatures has published a review of State Laws and Legislation Related to Biologic Medications and Substitutions of Biosimilars in 2019.⁴

In 2011, NCCN published a white paper (NCCN Biosimilars White Paper: Regulatory, Scientific, and Patient Safety Perspectives⁵) that addressed some of the concerns and challenges that were anticipated with the introduction of biosimilar medications, which impacted their adoption.^{6,7,8} Since 2018 a number of hematology/oncology biosimilar medications have become broadly available, and many more are approved (Table 1). The costs associated with these biosimilar medications are nearly always significantly less than the reference products, with discounts ranging from 10% to 50% relative to the reference product. This provides market competition and can result in lower costs to patients, healthcare systems and providers, and therefore to payors including Centers for Medicare & Medicaid Services (CMS). The combination of reduced cost and clinically irrelevant differences compared with reference products make the adoption of biosimilar products very enticing. However, there are several important observations that must be considered which make biosimilar products less than the universal panacea they were hypothesized during their inception. Safety, efficacy, manufacturer, and hospital and patient considerations must be assessed for consideration of the selection of biosimilars for formulary inclusion.⁹ An important issue that requires attention is the influence that relevant insurers or payors have in selection of the biosimilar medication.

Table 1. Reference/innovator and biosimilars in oncology (last updated: 1/26/21)

	SUPPORTIVE CARE			THERAPEUTIC		
CHEMICAL NAME	Epoetin	Filgrastim	Pegfilgrastim	Rituximab	Bevacizumab	Trastuzumab
INNOVATOR	Procrit	Neupogen	Neulasta	Rituxan	Avastin	Herceptin
BIOSIMILAR	Retacrit (epoetin alfa-epbx)	Nivestym (filgrastim-aafi)	Fulphila (pegfilgrastim-jmdb)	Ruxience (rituximab-pvvr)	Mvasi (bevacizumab-awwb)	Herzuma (trastuzumab-pkrb)
		Zarxio (filgrastim-sndz)	Nyvepria (pegfilgrastim-apgf)	Truxima (rituximab-abbs)	Zirabev (bevacizumab-bvzr)	Kanjinti (trastuzumab-anns)
		Granix* (tbo-filgrastim)	Udenyca (pegfilgrastim-cbqv)	Riabni (rituximab-arrx)		Ogivri (trastuzumab-dkst)
			Ziextenzo (pegfilgrastim-bmez)			Ontruzant (trastuzumab-dttb)
						Trazimera (trastuzumab-qyyp)
NUMBER OF BIOSIMILAR PRODUCTS UNDER INVESTIGATION	1	4	5	4	7	5

* Not a biosimilar for Neupogen

The scope of this position paper is to discuss the specific challenges when adopting biosimilar medications into practice. We have assembled a working group of pharmacy leaders from various NCCN hospitals, health systems, and centers. This working group was assembled in late 2019 and worked monthly to develop these recommendations. NCCN provided administrative support and oversight. This paper was designed around a biosimilar survey that was completed by the NCCN Pharmacy Directors Forum. The biosimilar survey included 14 respondents, representing the following institutions:

Table 2. Survey Respondents

Case Comprehensive Cancer Center/University Hospitals Seidman Cancer Center and Cleveland Clinic Taussig Cancer Institute, Cleveland, OH
City of Hope National Medical Center, Duarte, CA

Dana-Farber/Brigham and Women’s Cancer Care Center Massachusetts General Hospital Cancer Center, Boston, MA
Duke Cancer Institute, Durham, NC
Fred Hutchinson Cancer Center Research Center/Seattle Cancer Care Alliance, Seattle, WA
Mayo Clinic Cancer Center, Phoenix/Scottsdale, AZ; Jacksonville, FL; Rochester, MN
Memorial Sloan Kettering Cancer Center, New York, NY
The Ohio State University Comprehensive Cancer Center - James Cancer Hospital and Solove Research Institute, Columbus, OH
O’Neal Comprehensive Cancer Center at UAB, Birmingham, AL
The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD
Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine, St. Louis, MO
University of Wisconsin Carbone Cancer Center, Madison, WI
Vanderbilt-Ingram Cancer Center, Nashville, TN
Yale Cancer Center/Smilow Cancer Hospital, New Haven, CT

The survey included the eight questions in Table 3. The questions were answered using a 5-point Likert scale indicating the level of significance regarding operational challenges with biosimilar products (1 - not significant to 5 - very significant).

Table 3. NCCN Pharmacy Director’s Forum Survey – Rate according to scale 1 (not significant) to 5 (very significant)

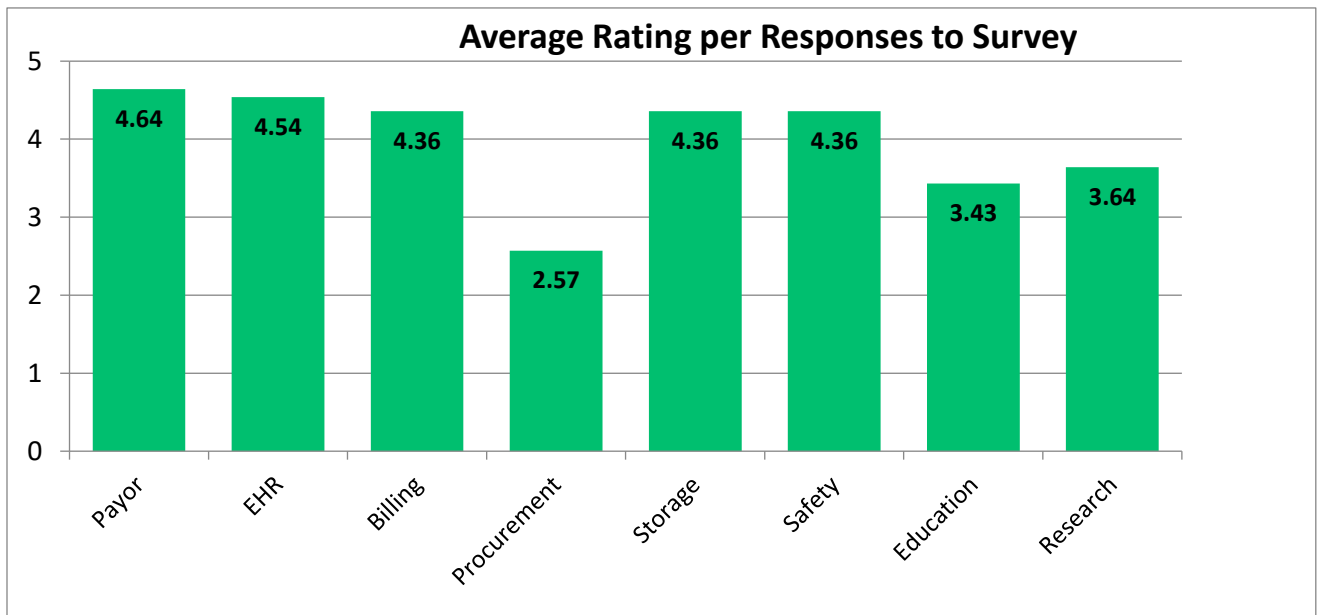
1) Payor restrictions to specific products
2) Leveraging the electronic health record (EHR) to identify specific payors
3) Coordination with the financial clearance unit to assure appropriate billing procedures (e.g. identification of denials prior to the patient’s treatment)
4) Procurement of the appropriate product(s) (e.g. availability and shortages)
5) Potential storage of multiple biosimilar products (e.g. if multiple payors selected various different products which would require multiple strengths from multiple manufacturers)
6) Ensuring patient safety with multiple available products (e.g. complexity of the operational system, also if multiple strengths from multiple manufacturers are required)
7) Education of non-pharmacy personnel on the appropriate use of biosimilars (e.g. provider, nurse, and patient education on what biosimilars are and how they are different than the innovator product)
8) Clinical trial requirements (e.g. the requirement for innovator vs. biosimilar and payment of medication as a part of a clinical trial)

The survey results are described in Figure 1. Five questions were identified to have an average score between somewhat significant and very significant, and in each of these questions $\geq 50\%$ of respondents indicated that these challenges were very significant. These highly scored questions

became the five area of focus for this position paper. Each of these areas was led by two section leaders from the NCCN Pharmacy Directors Forum. The section leaders were responsible for researching, collecting feedback from the other NCCN member institutions, and authoring each of the following sections.

- Patient safety (question 6)
- Payor restrictions to specific products (question 1)
- Leveraging the electronic health record (EHR) (question 2)
- Storage of multiple products (question 5)
- Coordination with the revenue cycle team (question 3)

Figure 1. Results of the NCCN Pharmacy Directors Forum Survey



Payor Restrictions:

As previously described, biosimilar medications receive FDA approval based upon demonstrating no clinically meaningful difference compared to the reference products; however, they cannot be treated as a traditional generic equivalent medication due to biologically-based manufacturing process differences that result in slight product variations. As such, these products cannot be easily

interchanged in the same manner as small molecule brand and generic drug products. Similarly, billing specifics and reimbursement are separate and distinct for each of these products. Each biosimilar product has its own distinct four-letter suffix code and requires its own Healthcare Common Procedural Coding System (HCPCS) billing code and billing unit equivalency. See Table 1 for currently (as known at this time) available biosimilar products used in hematology/oncology and those expected to be available. Some payors have mandated that providers prescribe a specific preferred product for their insured patients/covered lives membership population or reimbursement is at risk. The payor will specify a particular biosimilar product as being the preferred product and that other biosimilars are therefore “Not Medically Necessary” or “Do Not Meet Medical Necessity Requirements” unless or until the patient has received and is unable to tolerate the “preferred” biosimilar product. It is thought that a possible reason for these practices is that payors contract directly with manufacturers for specific products to reduce their cost by negotiating specific rebates which are not known to the general public.

Payor restrictions can threaten the continued availability of biosimilar products in the marketplace if payors refuse to reimburse for, without exclusions or restrictions, at parity, all biosimilar products within a therapeutic class. In some cases, certain payors require use of the higher cost (to the hospital) reference product, to the detriment of the less expensive biosimilar. In such cases, it is thought, similar to the cases referenced in the preceding paragraphs, that there may be hidden rebates shared only from the reference product manufacturer to the payor and not available to the actual health care provider or to the patient (in terms of decreased out of pocket responsibilities as specified by the payor).² We strongly recommend against single source mandates of biosimilar products by insurance companies for a variety of patient safety and operational reasons. As an illustrative example, in Table 4, BCBS of Illinois allows Avastin as the bevacizumab product and Herceptin, Kanjinti, or Ogivri as the trastuzumab product, whereas United Health Care prefers Mvasi as the bevacizumab product and Kanjinti as the trastuzumab product.

Table 4. Example of Payor Preferences

Chemical name*	Payor				
	Medicare (CMS)	Medicaid	Blue Cross Blue Shield Illinois	Aetna	United Healthcare
Rituximab	No preferences on products	All three products are non-preferred	Rituxan No medical policy on rituximab or Ruxience	Rituxan – “requires precertification” and considers rituximab medically necessary for certain criteria Truxima – “requires precertification” and considers rituximab medically necessary for certain criteria; preferred for FDA approved indications Ruxience – not on formulary	For all three products: benefit coverage determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service
Bevacizumab	No preference on products	Prefers Avastin Biosimilars are non-preferred	Avastin (in some cases required due to orphan status FDA approval for ovarian cancer)	Avastin and Mvasi are covered drugs	Prefers Mvasi
Trastuzumab	No preference on products	Prefers Herceptin Biosimilars are non-preferred	Prefers Herceptin or associated biosimilar (Kanjinti or Ogivri)	Herceptin and Kanjinti “requires precertification”; considers trastuzumab medically necessary for certain criteria	Prefers Kanjinti
<p>Disclaimer: Information in this table is correct to the best of our knowledge at the time of manuscript completion. It is subject to change as additional biosimilar products receive FDA approval and/or reach the marketplace, or as insurance companies develop new criteria for what they will allow to be reimbursed for patients for whom they are the current health care insurance provider.</p>					

*See Table 1 for details on available products

Conflicting preferences and restrictions by payors threaten the time-proven framework of institutional Pharmacy and Therapeutics (P&T) Committee formulary selection processes that will lead to significant challenges in adopting biosimilars, creating potential for confusion and errors when one payor mandates one brand of a medication for one patient and another payor mandates another brand for a second patient with the same diagnosis or clinical indication. Such challenges are based solely on insurance company restrictions, which are generally not visible to the physician or pharmacist and often are not known ahead of time by the Finance Department prior authorization (PA) or pre-certification (Pre-Cert) staff members. When PA is performed, the inevitable result is payment denial with resulting appeals, draining time and resources from healthcare providers and contributing nothing to improve patient outcomes or safety, or decreasing the cost of health care. Policies such as these may also lead to medication errors and/or financial toxicity for patients. Should some biosimilar manufacturers leave the market due to lack of parity and lack of equal access to hospitals (since hospitals cannot administer medications that they know will not be reimbursed), this may lead to less competition and possible loss of cost savings – the original reason for the BPCI Act. These practices could be construed as counter to the FDA’s Biosimilars Action Plan (BAP), which focused in part on identifying and highlighting anticompetitive behaviors that negatively impacted biosimilar competition. We encourage institutions and regional alliances of health care providers to reach out to legislators, governmental agencies, employers, and patients to help advocate against payors’ practices of allowing for reimbursement of only one biosimilar product.

Strategies for navigating the biosimilar payor landscape:

1. Maintain an up-to-date database of the biosimilar products available (illustrative examples in Table 4).

2. Meet with your Contracting and Payor Relations Department, managed care, and financial clearance (prior authorization/pre-certification) teams frequently.
3. In conjunction with your Contracting/Payor Relations Department, identify primary payors in your area and know which products each payor covers and if preferred agents are designated (Table 4). If possible, work with your institution's Contracting/Payor Relations Department to advocate with responsive payors for parity in reimbursement.
4. Require increased payor transparency regarding policy changes around biosimilars (via Congress and CMS).
5. Complete a financial analysis on each product, including:
 - a. Acquisition cost, off invoice wholesaler Cost of Goods discount, net acquisition costs, and potential rebates
 - b. Consider payor reimbursement (e.g., any "preferred status" policies/restrictions)
6. Communicate payor preferred/required product selections to clinicians for impacted patients when it requires action by the physician.
7. Negotiate with payors for reimbursement at parity.

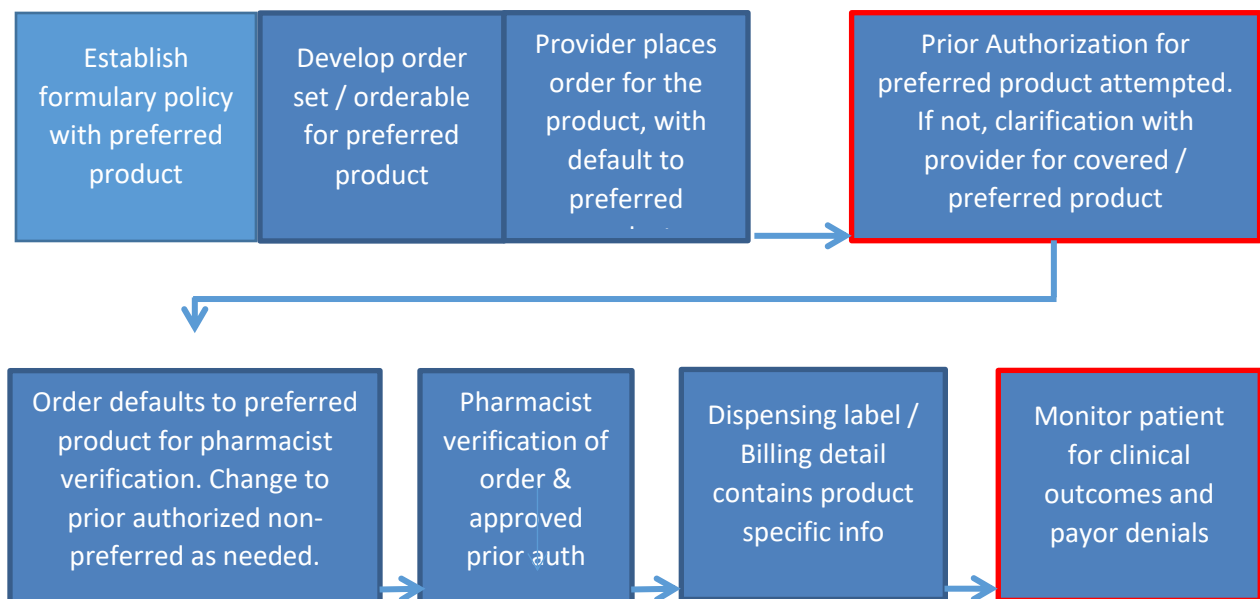
Coordination with Hospital Revenue Cycle Team:

Working with the institution's revenue cycle team is a key strategy to successful adoption of biosimilar products. As payors demand biosimilar use, and in some cases specific products, the Pharmacy Department should work closely with the PA or Pre-Cert Departments, to assure that the correct product is ordered and available for the patient. As a reminder, Fee For Service (conventional) Medicare does not provide PA and therefore the institution treats patients without knowing if reimbursement will occur. It is imperative that Pharmacy collaborate with the revenue cycle team on a regular basis. The revenue cycle process includes payor contracting, financial clearance, coding and

billing, and denial/appeal management. Depending on the institution, other departments may be included as part of the revenue cycle team. In some institutions, pharmacy performs PA for drugs in the infusion center; however, in other institutions the business or finance or patient billing department may be responsible. Wherever PA is completed, pharmacy must be included in communications regarding the approved biosimilar.

A suggested workflow for adopting biosimilar products is outlined in Figure 2.

Figure 2. Suggested workflow for biosimilar processing in an infusion center



This workflow assumes that the PA is not acquired on the same day as treatment. The workflow steps include:

1. Determine the preferred product for the institution. This would follow the institution's regular formulary process as governed by the P&T Committee. This process should also include considerations such as therapeutic equivalency, under what circumstances Pharmacy can perform a therapeutic interchange and the communications process necessary to let the clinical team know the product is being changed.

2. It is highly recommended that treatment plans, therapy plans, order sets, or other ordering process within the electronic health record (EHR), specifically stipulate the preferred product as the defaulted product on the order. Note: using the EHR to optimize biosimilar products is discussed in another section of this paper.
3. The order with the institution's preferred product is sent to the PA or Pre-Cert team once the treatment plan is applied.
4. The PA or Pre-Cert team reviews the patient's insurance and determines if a PA is required. There can be a gap here if a particular payor does not require or allow prior authorization for this particular drug; however, the payor may have established a medical coverage decision requiring a biosimilar or requiring a biosimilar by a particular manufacturer. The medical coverage decision will supersede a Prior Authorization or authorization waiver and the drug is at risk for denial. Thus, it is especially important that the PA or Pre-Cert team knows when a payor requires a biosimilar (rather than the reference product) or requires a specific biosimilar product.
5. If the PA or Pre-Cert team determines that the payor does not cover the institution's preferred product, communication back to the clinical team may be necessary. The next part of the workflow may be institution dependent.
 - a. Some institutions ask the PA or Pre-Cert team to get a PA for the product required by the payor and then send information for the order to be changed. If this is allowed, it creates less re-work and would be a recommendation.
 - b. Some PA or Pre-Cert teams may need an order for the correct product to complete the request for the PA and ask for an updated order prior to asking for a PA for the correct product. The process would require a change of the order to the correct product and then re-starting the PA process.

6. The PA or Pre-Cert team sends a message to the clinical team notifying them that the order needs changing. There are a couple of ways an institution can proceed at this point.
 - a. Have the provider change the order and re-send the PA request
 - b. Authorize Pharmacy to change the order through therapeutic interchange or standing orders. At this point, the PA request may or may not need to be re-sent, depending upon the actions of the PA or Pre-Cert team prior to requesting the original change from the clinical team. Using the hospital's or health system's therapeutic interchange policy, if state law allows, permits the biosimilars to be changed if the payor demands a product other than the institutions preferred product without needed provider input. Regardless of the processes that are followed, all state regulations must be observed and adhered to.
7. Revenue cycle team is monitoring for denials on the expensive drugs and follows up on the reason for denial. This information is sent to the business analyst and can be an opportunity for Pharmacy to collaborate on the root cause of denials. The tracking and analysis of denials is essential to learn where improvements can be made to prevent future denials.
 - a. Ideally, EHR systems will ultimately be capable of doing prior authorizations for infusion medications, much like the process with oral prescription medications in the pharmacy benefit. Until this is possible, it is essential the review process described be followed.

Biosimilar products create an opportunity for cost savings. As more payors are demanding biosimilar adoption with fewer demanding specific products, we believe if an institution has a biosimilar as the preferred product, the number of times a payor will demand a product change will be minimized. As described, the adoption of biosimilars requires additional work and may require additional resources in the PA or Pre-Cert team, other parts of the revenue cycle, or in Pharmacy. The Pharmacy and revenue cycle teams should work closely together to improve efficiencies and reduce duplication of efforts and improve efficiencies.

Patient Safety:

The cost savings benefit provided by market competition from development of biosimilars is not without additional considerations for patient safety. Many of the other discussed areas for institutional consideration in the expanded use of biosimilars have patient safety implications, including storage of biosimilars, use of the EHR in identifying payor preferences, and supply chain procurement. Ultimately, biosimilars have presented a unique set of patient safety challenges that are necessary to mitigate prior to expanded institutional use. This section serves to provide guidance in such a mitigation strategy.

Failure Modes and Effects Analysis (FMEA) has served as an effective method to prospectively evaluate procedures in order to recognize potential areas of failure and their associated effects. Review aspects in an FMEA include failure modes, failure causes, and failure effects that comprehensively identify what could go wrong, why the failure could happen, and what are the consequences of failure, respectively. This can aid in the improvement of procedures to help avoid preventable harm to patients by mistakes within a system. It is therefore recommended that institutions complete an FMEA on the utilization of biosimilars in order to identify mitigatable errors based on an individual institution's developed plan.

Table 5 is an example FMEA for patient safety concerns in the implementation of biosimilar procedures, most of which is discussed in further detail in other corresponding sections. Most of these process steps are universally applicable and should be considered in designing solution strategies. An example of a step in the biosimilar process is that of patient administration. The failure mode for this step in the process would be incorrect product manipulation, likely caused by human error. This is a plausible error as biosimilars are manufactured in a variety of delivery systems including prefilled syringes, vials, or injectable pens. Different product types have become increasingly common as manufacturers work to differentiate their product from others on the market. This failure effect could range from incorrect administration to the patient experiencing an adverse event. Based on this

evaluation, it is up to the individual institution to provide correcting factors to anticipate and prevent these errors from occurring that are best able to be consistently implemented within this step of the process. This may include institutional administration guidelines for each biosimilar, utilization of the EHR to provide administration resources, and extensive personnel training.

While Table 5 serves as a comprehensive example of an FMEA, best practice would be to perform one on an individual institutional level. This analysis should also be iteratively performed as additional biosimilars come to market, convoluting the already complex available products.

Table 5. Failure Modes and Effects Analysis (FMEA)

Item or Process Step	Failure Mode	Effect	Cause	Current Control
Supply Chain Procurement	Ordering Error	Procuring Incorrect Product	Manual Ordering (i.e. human error)	Spell Check
	Inability to Obtain Product from Distributor	Delayed Patient Care	Ability of Distributor to Procure Product	Automated Ordering
Storage of Inventory	Pulling Incorrect Product	Administering/Billing for Incorrect Product	Manual Pulling (i.e. human error)	Dispense Preparation
	Lack of Physical Space	Delayed Patient Care	Space Capacity	
Prescribing Based on Payor	Claim Submission Denial	Delayed Patient Care	Payor Regulation	
	Payor Designation of Only One Product	Requirement for Multiple Products on Inventory	Manual Communication, Manipulation, and Documentation (i.e. human error)	
	Lack of Handoff Communication (i.e. OP/IP)	Administering/Billing for Incorrect Product		
	Discharge Reconciliation Error	Therapy Duplication		
EHR to Identify Payor	Reimbursement Plan Unknown	Claim Denial with Need for Re-Submission	Lack of Transparency	
Provider or Pharmacist Ordering in EHR	Error Due to Defaulting Reference Product	Administration/Billing for Incorrect Product	Automated Default	
	Error Due to Site of Care Nuances (i.e. date/time sensitive)	Delayed Patient Care	Manual, Manipulation and Documentation (i.e. human error)	
	Error in Manual Modification to Select Biosimilar	Patient Inconvenience		

Dispensing and Checking	Lack of technology (e.g. Dispense Prep/Epic) Incorrect Quantity (i.e. each or kit) Lack of Standardization for Vial Sizes and Concentration	Administering/Billing for Incorrect Product Administering/Billing for Incorrect Quantity Administering/Billing for Incorrect Drug Amount	Manual Manipulation (i.e. human error) Lack of Manufacturing Standardization	Dispense Preparation Pharmacist Product Checking
Patient Administration	Incorrect Product Manipulation (i.e. prefilled syringe vs. vial vs. pen)	Administration Error Patient Adverse Event	Manipulation (i.e. human error)	
Charging with Billing Code	Incorrect J Code Association	Reimbursement Denial Patient Financial Burden	Automated Billing	

Leveraging the Electronic Health Record (EHR) to support biosimilar adoption:

With the rapid approval of biosimilar agents, organizations are challenged to create EHR solutions to clearly distinguish between multiple medication records for the same reference product. Unlike brand and generic interchangeability, biosimilar products are unique and have a different naming structure. As a result, one medication record does not suffice. To further complicate matters, payors are preferential to which biosimilar agent will be covered and, hence, which HCPCS code can be billed. For some reference products such as trastuzumab, there are already five FDA approved biosimilar agents to manage: trastuzumab-dttb (Ontruzant), trastuzumab-pkrb (Herzuma), trastuzumab-qyyp (Trazimera), trastuzumab-anns (Kanjinti), and trastuzumab-dkst (Ogivri). The responsibility for maintaining these medication records as well as managing payor mandates often falls on the verifying pharmacist. Therefore, it is essential to optimize the EHR and streamline the process of patient PA approval, record management, and order verification. Recommendations for how to achieve this are discussed throughout this section using two EHR platforms – EPIC and Cerner.

Notifying end-user of payor mandates:

Often, the verifying pharmacist is responsible for ensuring the correct biosimilar agent is selected based on payor preference. Depending on whether the PA team for the infusion is internal or external to pharmacy, communication of a payor mandate and need to select a specific biosimilar agent can vary. Based on an abbreviated survey of NCCN pharmacy directors, mandate notifications can be in form of email, phone call, daily huddle, documentation in EPIC referrals, in-basket message, and/or instant message. To support universal communication and visibility across all teams, documentation within the EHR is the preferred method of communication.

Within the EPIC system, the referrals tab is commonly used to note other authorizations such as clinical appointments procedures and take-home prescription medications. Since this tab is visible to all disciplines, documentation of a biosimilar mandate within the referral would be ideal. The verifying pharmacist can then reference and use this communication to select the correct biosimilar agent. While the prior authorization team will need to regularly update and maintain the referral, for example when patient insurance changes or for payor mandate fluctuations, it is the most universal means to communicate and ensure all parties are on the same page.

Another means to alert the verifying pharmacist of a biosimilar mandate can be through a banner alert or automatic notification through a pre-defined payor rule. In this case, when the patient's chart is opened, an alert appears, highlighting the need for a specific payor. The verifying pharmacist then uses a reference tool to determine which biosimilar agent to select and verify. While this method may lead to alert fatigue, it is an easy method to ensure the end user is consistently notified. Similar to the referrals tab, the alert banner will need to be maintained based on patient insurance changes and payor mandates. Pictured in Figure 3 below is a screen shot highlighting a financial authorization request – specific product alert banner.

Figure 3. Example of a Financial Authorization Request – Specific Product Alert Banner.

Location: [REDACTED] HEIGHT: [REDACTED] DOSING WT: [REDACTED]
 Fin# [REDACTED] Plan:BCBS Florida Medicare AdvantageCODE:No Code

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For a pre-defined payor rule, the treatment plan will automatically default to the payor’s preferred agent. This is based on rule functionality and advanced order groups that are defined for EPIC platforms only. Advanced order groups are defined in more detail below.

Manipulating Patient Treatment Plans:

Once the end user is notified, the patient’s treatment plan (whether within Beacon or another plan) needs to be manipulated to reflect the correct biosimilar. While some NCCN organizations opt to maintain individual medication records, some EPIC institutions have opted to utilize Advanced Order Groups (AOGs). These still require separate medication records for each biosimilar but allows for easier interchangeability between agents.

In short, an AOG within EPIC “lives” in the background of any Beacon or therapy plan. As pictured below in Figure 4, agents for the same reference product are grouped together with one agent defaulting as preferred. At the time of verification, the pharmacist is able to quickly edit the plan and select the correct agent. This eliminates the need for the medication record to be deleted and “swapped out” with another.

Figure 4. Example of an Advanced Order Group (AOG)

The screenshot shows a treatment plan for 'UWH ADULT HEMONC PEGFILGRASTIM EVERY 2 WEEKS'. It details treatment conditions and medications. Under 'Treatment Medications', there is an AOG for Pegfilgrastim with two options: Fulphila (selected) and Neulasta.

Interval	Defer until	Duration
Every visit	S	Until discontinued
Every visit	S	Until discontinued
Every 14 days	S	Until discontinued
Every 14 days	S	Until discontinued

Permission granted to share from EPIC

Whether an AOG is utilized or a medication record is maintained, manipulating a patient's treatment plans is a high-touch process. All NCCN pharmacy directors recommend a second pharmacist check of plan manipulation before the treating provider signs and releases the order.

Overall, there are many strategies to consider when building biosimilar records into the EHR. The key is for the end user to understand which record is needed due to payor mandates. While tedious, this action is vital for authorization and reimbursement as described in that section.

Storage of Multiple Biosimilar Products:

There is increased concern over the storage of biosimilar products as more products come to market. As described previously the practice that many payors are designating different products on their formulary with preferred status is also leading to increased strain on inventory and the risk of medication errors.¹⁰ A variety of strategies can be considered to help alleviate some of these concerns. One strategy is to stock multiple biosimilar products. This approach ensures the appropriate product is available for the patient. However, this strategy may increase carrying costs, and place a strain on storage requirements such as refrigerators, freezers, and negative pressure storage space. Another concern is the potential for dispensing errors, as multiple similarly named products are stored on hand.

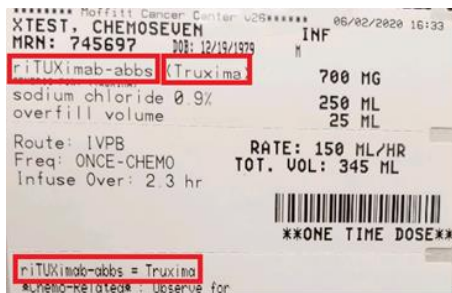
An alternative strategy that improves storage concerns and limits the potential for dispensing errors is to establish a single preferred biosimilar product. One of the major challenges associated with stocking a single product is negotiating this strategy with the payors, either directly or indirectly, in an attempt to ensure the majority of payors for patients seen at the institution prefer the same biosimilar. This can be particularly challenging at large institutions that treat patients throughout the region and country. To successfully utilize this strategy, a method must be put in to place to identify patients/payors that require a biosimilar that is not routinely stocked by the organization. This will help to ensure patient specific medications are proactively ordered for those patients that require the non-preferred product.

Despite some of the challenges associated with stocking a single, preferred biosimilar product, the NCCN Pharmacy Directors Forum recommends this strategy. Institutions should work with payors (directly or indirectly) to allow a preferred product to limit strain on inventory and the potential for medication errors. Special procedures should be developed to order patient specific medication for those patients that require a biosimilar that is not routinely stocked.

Physical Inventory Considerations:

Regardless of the decision to stock multiple biosimilar products versus a single biosimilar, there is still a need for managing increased inventory within the pharmacy to ensure safe dispensing and administration of medications. Similarities in naming convention is a major concern with the biosimilar products as nonproprietary names differ only by a unique suffix. As a result, each product should be stored based on the proprietary name with the nonproprietary name and unique suffix also present (see Figure 5). Products should be searchable and labeled by both nonproprietary name and suffix and the proprietary name to help avoid confusion and difficulty identifying the appropriate product. Additionally, bar code scanning should be utilized throughout the entire medication use process to facilitate safe dispensing and administration. This should start from the medication’s point of entry into the pharmacy and continue all the way to the point of administration.

Figure 5. Example of Product Labeling



It is recommended that institutions routinely monitor notices and alerts from the Institute for Safe Medication Practices (ISMP) in order to identify any new safety concerns associated with biosimilars, and reference the list of confused drug names to prevent medication errors. ISMP has

already reported look-alike errors between Prolia (denosumab) and Udenyca (pegfilgrastim-cbqv) due to similarly designed boxes that both require storage under refrigeration.¹¹ Institutions should make every effort to proactively identify new products that could result in look-alike errors and modify storage appropriately before procurement or adding to the formulary. Configure storage cabinets and locations to prevent look-alike and/or sound-alike medications from appearing consecutively and utilize tall man lettering for look-alike product names. If these steps are not possible, consider circling the drug name on the product to avoid medication errors.

Figure 6. Example of Look-Alike Error Between Prolia (denosumab) and Udenyca (pegfilgrastim-cbqv)



Use of Automation with Multiple Biosimilar Products:

Many centers are using multiple forms of advanced technology to store, compound, and administer intravenous medications. The use of multiple biosimilars can put significant strain on infusion centers and institutions as each product must be loaded and maintained in the drug libraries associated with each system. This can be extremely time consuming and requires working with multiple vendors. As a result, automation solutions may not be available for each biosimilar, thereby increasing the risk of medication errors. Institutions have a few options when determining how they want to configure smart pumps and their drug libraries. A unique library entry can exist for each product based on the proprietary name or a single drug library entry can exist for the reference product and each biosimilar. A unique entry for each biosimilar can lead to an extensive library and confusion due to multiple entries with the same biosimilar. Additionally, this can be significantly more time consuming to

manage. A single drug library entry can save time and consolidate the library. When utilizing this strategy, institutions should ensure the same guardrails and infusion parameters exist between products. Regardless of the method that best suits each institution, the panel recommends not dispensing a new biosimilar until all automation has been established including smart pump configuration, drug library storage, and appropriate compounding technology.

Conclusion:

The evolving world of biosimilar medications in oncology has several positive components. At the same time, however, there are concerns associated with biosimilar adoption that outweigh the benefit. Organizations need to be prepared to support biosimilar adoption from an operational and clinical standpoint before financial benefits can be achieved. The NCCN Pharmacy Directors Forum strongly advocates for constant vigilance, communication and collaboration between ancillary services (e.g. medical staff, revenue cycle, prior authorization, information technology) to ensure safe practices are maintained and biosimilars are successfully adopted.

The NCCN Pharmacy Directors Forum – Biosimilar Work group recommends the following as best practices for managing biosimilars:

1. Work with your payor relations group to establish parity for biosimilars. If possible work at a legislative level to push for biosimilar parity. The institution should demand transparency from payors.
2. Maintain a database of payors' biosimilar demands. Where parity is not achieved, document which payor is demanding specific products, which ones allow biosimilars but not the reference product, and which ones allow the reference product.
3. Using the institution's formulary process, determine a preferred biosimilar for the institution based upon efficacy, safety, cost, and convenience to the institution and patient.

4. Using the EHR, make the preferred biosimilar the defaulted product in treatment plans, therapy plans, order sets, or any other ordering processes.
5. Work with the revenue cycle group to determine a workflow that minimizes re-work and assures the patient is receiving a product that the payor will reimburse.
6. Use the Pharmacy & Therapeutics Committee-approved therapeutic substitution process to allow pharmacy to adjust the medications will help reduce the workload to providers.
7. Assure that the PA or Pre-Cert team, pharmacy personnel, and the revenue cycle team work together to monitor biosimilar use, identify payors making specific demands, and follow up on denials to find ways to improve the process.
8. Utilize a FMEA process to determine potential safety issues in using biosimilars. Use the information from the FMEA to improve the workflow and biosimilar processes to reduce the chance the patient receives a product that will not be reimbursed.
9. Leverage the EHR to drive change by defaulting the preferred product in orders. However, work to make the process of identifying when a biosimilar needs to be changed due to payor demand easy to see and easy to change. Utilize tools within the EHR, such as advanced order sets, to make the process simple.
10. Determine how the biosimilars will be stored safely and in such a manner that the correct product will be given to the patient for each dose. Utilize barcode technology as much as possible to reduce the risk of the wrong product being used.

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Authors:

1. Kenneth Komorny (**co-lead**), Moffitt Cancer Center
2. Ryan Roux (**co-lead**), The University of Texas MD Anderson Cancer Center
3. Sylvia Bartel, Dana-Farber/Brigham and Women's Cancer Center
4. Heather Jones, Cleveland Clinic Taussig Cancer Institute
5. Julie Kennerly-Shah, The Ohio State University Comprehensive Cancer Center - James Cancer Hospital and Solove Research Institute
6. Dwight Kloth, Fox Chase Cancer Center
7. Timothy Kubal, Moffitt Cancer Center
8. Mary Golf, Robert H. Lurie Comprehensive Cancer Center of Northwestern University
9. William Greene, St. Jude Children's Research Hospital
10. Patrick McBride, Dana-Farber/Brigham and Women's Cancer Center
11. Marissa Olson, Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine
12. Shawn Osborne, Case Comprehensive Cancer Center/University Hospitals Seidman Cancer Center
13. Jennifer Smith, Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine
14. Scott Soefje, Mayo Clinic Cancer Center
15. Colleen Timlin, Abramson Cancer Center at the University of Pennsylvania

NCCN:

Evelyn Handel

Wui-Jin Koh

Leslie Ray (until November 2020)