Preparing for the market entry of adalimumab biosimilars in the US in 2023: A primer for specialty pharmacists

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Purpose: The impact of the market entry of adalimumab biosimilars on clinical practices and specialty pharmacies is explained. A roadmap is also provided for how pharmacists can successfully navigate this landscape.

Summary: Biosimilars have previously been introduced as a mechanism to help curb biologic expenditures, with biosimilars undergoing an abbreviated regulatory approval process that focuses on biosimilarity and generating product competition. Adalimumab is currently the leading product in the biologics market, generating approximately $20 to $30 billion in sales worldwide consecutively from 2019 to 2021. Many adalimumab biosimilars are slated to enter the market in 2023 and become available for patient use. However, compared to other biosimilars, adalimumab biosimilars have several unique considerations, such as interchangeability and concentration, that will impact pharmacy practices and workflows. Because pharmacists embedded in clinical practices and specialty pharmacies will be significantly involved in the processes relating to adalimumab biosimilar implementation, adoption, and use, a primer on understanding the various adalimumab biosimilar products available and considerations surrounding these products with regard to workflow and patient use is critical. Several resources are also provided to help pharmacists successfully navigate the adalimumab biosimilar landscape.

Conclusion: The biosimilar landscape continues to evolve, and 2023 will see the launch of several adalimumab biosimilar products, which vary with regard to formulation, concentration, and interchangeability status. Pharmacists are well positioned to educate providers and patients about this landscape and help implement an efficient workflow to support adalimumab biosimilar adoption and use.

Keywords: adalimumab, biosimilars, inflammatory conditions, specialty pharmacy, switching

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Biologic therapy has revolutionized the management of many chronic conditions and optimized patients' outcomes, inducing and maintaining disease control while improving quality of life. However, despite being clinically impactful, biologic therapies such as adalimumab, certolizumab, and etanercept are costly, with annual net costs of more than $30,000.[1] Biologic therapy has previously been estimated to account for 48% of net manufacturer revenue and 43% of total prescription spending.[2] These costs ultimately contribute to increased prescription drug expenditure and negatively impact various stakeholders such as insurers, insured members, and uninsured individuals, resulting in formulary restrictions, premium increases, and limited treatment access.[3]

Biosimilars are biologic products that are highly similar to an existing Food and Drug Administration (FDA)–approved originator (or reference)

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biologic product with no clinically meaningful differences in safety, purity, or potency. They were introduced as a mechanism to help curb the costs of biologic therapy by generating product competition and increasing treatment access and options.[1,4] Biosimilars undergo an abbreviated, but rigorous, pathway for FDA approval in which data from analytical, animal, and clinical studies demonstrating biosimilarity between the proposed biosimilar product and the reference product are reviewed. If biosimilarity is demonstrated and sufficient scientific justification is provided, biosimilars can be approved for additional indications held by the reference product without requiring direct clinical trials for those indications through a process of extrapolation.[4] Additional cost savings are generated with this process, as expensive and time-consuming clinical studies are not required given that the active ingredient in the biosimilar and reference product is the same. It is anticipated that biosimilars can generate cost savings of $38.4 billion (5.9% of total projected expenditures on biologics) between 2021 and 2025.[5]

In 2023, more than 5 biosimilars for adalimumab are anticipated to enter the market.[4] Adalimumab was approved by FDA in 2002 for the treatment of rheumatoid arthritis and, in subsequent years, gained approval for the treatment of additional conditions, including plaque psoriasis, psoriatic arthritis, ankylosing spondylitis, hidradenitis suppurativa, inflammatory bowel disease, and uveitis.[6] Given its early introduction and numerous indications, adalimumab has emerged and maintained its status as a leading biologic, generating approximately $20 to $30 billion in sales worldwide in 2019 to 2021.[2,7] Additionally, adalimumab has undergone several changes since its market launch, including introduction of pens and syringes that contain a lower concentration without citrate or latex and have smaller needle gauges. These product changes have generated additional patents, some of which will not expire until 2037.[8] These components introduce several additional considerations pertaining to adalimumab biosimilar formulation and concentration, which will be discussed herein.

KEY POINTS

- In 2023, several adalimumab biosimilars from different manufacturers are anticipated to enter the US market for patient use.
- Interchangeability designation and automatic substitutions will potentially help improve biosimilar adoption, contingent on state pharmacy laws.
- Pharmacists are well positioned to help oversee the integration of adalimumab biosimilars into patient care, for which a roadmap of workflow considerations is provided.

To prepare pharmacists for this upcoming transition, we provide a primer on specific considerations relating to adalimumab biosimilars and tips on implementing an ideal workflow to successfully support biosimilar adoption and switching. It is important that pharmacists in all practice settings understand the biosimilar landscape so that they can make informed decisions in accordance with patients' insurance requirements. Formularies, pharmacy networks, prior authorization requirements, and copay tiers can differ widely among insurance plans, and decisions should be made on a patient-by-patient basis. Health-system specialty pharmacies are well positioned to effectively manage the transition to biosimilars due to their integration with patients and providers, access to the electronic health record (EHR) and secure digital patient communication tools, and influence on therapeutic decision-making through collaborative practice agreements.[9,10]

Lessons learned with biosimilar implementation

Prior implementation experiences have largely been with noninterchangeable clinic-administered biosimilars. Even so, there are lessons to be learned and best practices to adopt. Kar et al[11] credited their success in implementing 5 different biosimilars to clear communication with stakeholders and development of a strategic, deliberate multidisciplinary process for managing formulary, safety, and operational barriers. Bhat et al[12] successfully transitioned 97% of eligible patients to infliximab-dyyb without compromising clinical outcomes. As part of the implementation process, the pharmacy team prepared patient education materials and contacted each patient directly by telephone with scripted talking points to discuss the biosimilar transition. Additionally, the transition process was standardized by switching patients after 6 months of receiving the reference medication and through careful identification of eligible patients. Lam et al[13] performed planned evaluations of patients' experiences after the change to a biosimilar to assess the implementation's success and real-world patient outcomes. This also allowed for comparison of biosimilars preferred by different payors.

The transition to self-administered, interchangeable biosimilars such as insulin glargine-yfgn has been complicated by the influence of pharmacy benefits, including multiple insurance payors and sponsors, rebate incentives, and pharmacy benefit management drug formularies and contracts that dictate which products are reimbursed and the amount of reimbursement. Within 4 months of its approval, interchangeable insulin glargine-yfgn captured over half of all new prescriptions for insulin glargine and 15% of the total insulin glargine prescription market.[14] When it is favorable to the patient and permissible by state law, pharmacists have an option to substitute the biosimilar for the reference product, similar to the substitutions made for traditional generics. Best practices for pharmacists include understanding managed care decisions that dictate reimbursement and cost to the patient, accurately identifying

when a biosimilar can be substituted for a reference product, identifying eligible patients, and providing enhanced counseling and patient education. Uninsured patients may benefit from the lower cash price of the biosimilar. As patients become more aware of biosimilars, they may help to drive substitution by asking their pharmacist about safe, effective, and lower-cost options.

Adalimumab biosimilar products

At the time of writing, there were 8 FDA-approved adalimumab biosimilar products.[4] Details of these products, including biosimilar name, manufacturer, FDA approval date, expected market launch, formulations, and inactive ingredients, are provided in Table 1.[15-29] It is important to note that there is variability in concentration, needle size, and formulation among the adalimumab biosimilars when these are compared to each other and to reference adalimumab. In July 2019, reference adalimumab was reformulated from 40 mg/0.8 mL to 40 mg/0.4 mL. With this new formulation, the citrate buffer was removed and the injection volume and needle size were reduced. These changes led to reduced injection site–related pain and improved treatment adherence and persistence.[30,31] Because of high satisfaction with the adalimumab citrate-free 40 mg/0.4 mL formulation, most patients are not willing to switch to the old 40 mg/0.8 mL formulation. Thus, it is important to recognize the impact of the citrate-free 40 mg/0.4 mL formulation, as this may potentially influence biosimilar uptake, depending on product features.

As patients may be subjected to single or multiple transitions between adalimumab products (either reference to biosimilar or biosimilar to biosimilar), being familiar with each adalimumab biosimilar product and confidently counseling on these variabilities will help minimize patient confusion or mistrust. As of January 2023, FDA approval was pending for 3 additional adalimumab biosimilars.[32] The FDA website with biosimilar product information and Purple Book are excellent resources to stay up to date on emerging adalimumab biosimilar products.[4,33,34]

Interchangeability

Despite the large number of FDA-approved biosimilars currently on the market, only 2, insulin glargine-yfgn and adalimumab-adbm, have been deemed interchangeable by FDA.[34] Interchangeability permits pharmacists to substitute an interchangeable biosimilar product for a prescription written for the reference product without requiring intervention from the prescriber. To obtain interchangeability status for their biosimilar products, manufacturers must perform additional studies showing no difference in clinical and safety outcomes for patients switching between the reference product and the biosimilar multiple times.[4]

The interchangeability designation for adalimumab-adbm, which was granted in October 2021, was based on findings from the phase 3 VOLTAIRE-X clinical trial.[18,35-37] In this double-blind, multicenter, parallel-group randomized controlled trial, participants with chronic plaque psoriasis were initiated on adalimumab reference product 40 mg/0.8 mL (with a dose of 80 mg subcutaneously on day 1, followed by 40 mg every other week) for 14 weeks, and those who responded were then randomized to either (1) continue adalimumab reference product or (2) switch to adalimumab-adbm at week 14 to 16, switch to adalimumab reference product at week 18 to 20, and then transition back to adalimumab-adbm for weeks 22 to 48. No meaningful clinical differences in pharmacokinetics, efficacy, safety, or immunogenicity were noted between the multiple-switching and continuous treatment arms.

The implications of an interchangeability designation in clinical practice and patient care will be interesting to observe, as it is anticipated that payors and health systems will likely favor adding interchangeable biologics to the formulary notwithstanding cost barriers. However, application of interchangeability at the pharmacy level is contingent on state pharmacy laws (Table 2).[4,38] Specific rules may exist regarding whether a substitution can occur without prescriber approval, what must be communicated back to the prescriber and/or patient, and the timeframe when such communication must occur. Of note, if a prescriber marks "dispense as written" or "brand medically necessary" on the prescription, substitution with the interchangeable biosimilar is not permitted. As the landscape of biosimilars and laws around dispensing continue to evolve, it is pertinent for pharmacists to stay up to date with their specific state's rules and regulations as these are subject to change. In cases where pharmacies deliver medications to patients residing in other states, the pharmacy must ensure it is following the relevant pharmacy laws in the patient's state of residence. Furthermore, current FDA criteria do not permit substitution of 40 mg/0.4 mL citrate-free adalimumab reference with adalimumab biosimilars that are 40 mg/0.8 mL due to concentration differences.

Health-system specialty pharmacies with a pharmacy and therapeutics (P&T) committee may also be affected by these considerations, given their management of outpatient clinic formularies and/or health plans for their own employees. The P&T committee could potentially select a single interchangeable adalimumab biosimilar (due to cost considerations, as a means to decrease inventory cost, because of limited storage space or concern for medication errors, etc). Although in theory this may sound beneficial, it is currently unclear whether this is a feasible strategy in the outpatient setting as the choice of adalimumab biosimilar will be dictated by the insurer irrespective of other considerations.

Implementation and workflow considerations

Patients and providers should utilize shared clinical decision-making

Table 1. Adalimumab Biosimilar Products (FDA Approved)

	Adalimumab-atto (Amjevita)	Adalimumab-bwwd (Hadlima)	Adalimumab-adbm (Cyltezo)	Adalimumab-aqvh (Yusimry)	Adalimumab-fkjp (Hulio)	Adalimumab-adaz (Hyrimoz)	Adalimumab-afzb (Abrilada)	Adalimumab-aacf (Idacio)
Manufacturer	Amgen	Organon/Samsung Bioepis	Boehringer Ingelheim	Coherus Bio-Sciences	Viatris	Sandoz	Pfizer	Fresenius Kabi
FDA approval date	Sep. 2016	Jul. 2019	Aug. 2017	Dec. 2021	Jul. 2020	Oct. 2018	Nov. 2019	Dec. 2022
Expected launch date	Jan. 2023	Jul. 2023	Jul. 2023	Jul. 2023	Jul. 2023	Sep. 2023	Nov. 2023	Jul. 2023
Interchangeable	No	No	Yes	No	No	No	Pending	No
Diseases studied in clinical trials	RA, PsA[15]	RA[16,17]	CD, RA, PsA[18-21]	PsA[22]	RA[23,24]	RA, PsA[25,26]	RA[27-29]	Not available
Product characteristics								
Formulation	• SureClick autoinjector (40 mg) • Prefilled glass syringe	• PushTouch autoinjector • Prefilled glass syringe	Prefilled glass syringe	Prefilled glass syringe	• Pen (40 mg) • Prefilled plastic syringe	• Sensoready pen • Prefilled glass syringe with BD UltraSafe Passive needle guard	• Pen (40 mg) • Glass vial (40 mg) for institutional use only • Prefilled glass syringe	• Pen • Prefilled glass syringe
Concentration	40 mg/0.8 mL, 20 mg/0.4 mL, and 10 mg/0.2 mL	40 mg/0.8 mL	40 mg/0.8 mL and 20 mg/0.4 mL	40 mg/0.8 mL	40 mg/0.8 mL and 20 mg/0.4 mL	40 mg/0.8 mL	40 mg/0.8 mL, 20 mg/0.4 mL, and 10 mg/0.2 mL	40 mg/0.8 mL
Needle length	1/2 inch	1/2 inch	1/2 inch	1/2 inch	1/2 inch	1/2 inch	1/2 inch	1/2 inch
Needle size	27 (pen) or 29 (PFS)	29	27	Unknown	29	27	29	29
Contains latex	Yes	No	Yes	No	No	Yes	No	No
Citrate free	Yes	No	Yes	Yes	Yes	No	Yes	Yes
Stability at room temperature	14 days	14 days	14 days	14 days	14 days	14 days	30 days	28 days

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Inactive ingredients	Glacial acetic acid, sucrose, polysorbate 80, and water for injection (sodium hydroxide added as necessary to adjust the pH to 5.2)	Citric acid monohydrate, L-histidine, L-histidine hydrochloride monohydrate, polysorbate 20, sodium citrate dihydrate, sorbitol, and water for injection	Glacial acetic acid, polysorbate 80, sodium acetate trihydrate, trehalose dihydrate, and water for injection	Glycine, L-histidine, L-histidine hydrochloride monohydrate, polysorbate 80, sodium chloride, and water for injection, USP (sodium hydroxide added as necessary to adjust the pH)	Methionine, monosodium glutamate, polysorbate 80, sorbitol and water for injection (hydrochloric acid added as necessary to adjust pH)	Adipic acid, citric acid monohydrate, mannitol, polysorbate 80, sodium chloride, and water for injection	Edetate disodium dihydrate, L-histidine, L-histidine hydrochloride monohydrate, L-methionine, polysorbate 80, sucrose, and water for injection	Glacial acetic acid, polysorbate 80, sodium chloride, trehalose, and water for injection (sodium hydroxide added as necessary to adjust the pH)

Abbreviations: CD, Crohn's disease; FDA, Food and Drug Administration; PFS, prefilled syringe; PsA, plaque psoriasis; RA, rheumatoid arthritis.

when initiating treatment with adalimumab, and biosimilar education ideally occurs during these encounters. Once adalimumab biosimilars enter the market, clinicians will be faced with a disruption to previously established workflows relating to adalimumab initiation and continuation. In addition, they will be subjected to additional considerations pertaining to adalimumab therapy access, the payor landscape, and formulary preferences. Pharmacists, embedded in both specialty clinics and specialty pharmacies, may already have a role in the initiation and management of patients on adalimumab; however, their role will expand into managing biosimilar medication access and counseling as adalimumab biosimilars become available. Specific considerations relating to adalimumab biosimilar implementation and workflow considerations are discussed below and summarized in checklists (Figure 1). The checklists are designed to outline relevant tasks and considerations for staff embedded in pharmacies and/or specialty clinics (eg, gastroenterology, rheumatology, and dermatology clinics) to prepare for the launch and adoption of adalimumab biosimilars in practice.

Adalimumab prescription order entry. Given the advance notice that these products are on the horizon, preparation and coordination with information technology teams to introduce EHR and pharmacy software ordering/processing capabilities should be undertaken as soon as possible to ensure seamless order entry and mitigate potential treatment delays. As most prescriptions originate from the EHR, prescriptions relating to new starts should continue to be annotated as "adalimumab" to allow for interchangeable substitution per formulary preference. If substitution via interchangeability is permitted, this will help minimize treatment delays on the pharmacy side as a new prescription will not be needed to dispense the preferred adalimumab biosimilar product. Conversely, pharmacists will need to prepare for increased

Table 2. State Pharmacy Rules Regarding Interchangeability[38,a]

	State law specific to interchangeability of biologics	Substitution permitted without prescriber approval	Must communicate substitution to the prescriber	Must communicate substitution to the patient
Alabama	Yes	No	Yes	Yes
Alaska	Yes	Yes	Yes	Yes
Arizona	Yes	Yes	Yes	Yes
Arkansas	Yes	Yes[b]	Yes	Yes
California	Yes	Yes	Yes	Not specified
Colorado	Yes	Yes	Yes	Yes
Connecticut	Yes	Yes	Yes	Yes
District of Columbia	Yes	Yes	Yes	Yes
Delaware	Yes	Yes	Yes	Yes
Florida	Yes	Yes	Yes	Yes
Georgia	Yes	Yes	Yes	Yes
Hawaii	Yes	Yes	Yes	Yes
Idaho	Yes	Yes	Yes	Yes
Illinois	Yes	Yes	Yes	Yes
Indiana	Yes	No	Yes	Yes
Iowa	Yes	Yes	Yes	Yes
Kansas	Yes	Yes	Yes	Yes
Kentucky	Yes	Yes	Yes	Yes
Louisiana	Yes	Yes	Yes	Not specified
Maine	Yes	Yes	Yes	Yes
Maryland	Yes	Yes	Yes	Yes
Massachusetts	Yes	Yes	Yes	Yes
Michigan	Yes	Yes	Yes	Yes
Minnesota	Yes	Yes	Yes	Yes
Mississippi	Yes	Yes[b,c]	Yes	Yes
Missouri	Yes	Yes	Yes	Yes
Montana	Yes	Yes	Yes	Not specified
Nebraska	Yes	Yes	Yes	Yes
Nevada	Yes	Yes	Yes	Yes
New Hampshire	Yes	Yes	Yes	Yes
New Jersey	Yes	Yes	Yes	Not specified
New Mexico	Yes	Yes	Yes	Yes
New York	Yes	Yes	Yes	Yes
North Carolina	Yes	Yes[b]	No	Not specified
North Dakota	Yes	Yes	Yes	Yes
Ohio	Yes	Yes[b]	Yes	Yes
Oklahoma	Yes	Yes	Yes	Yes
Oregon	Yes	Yes	Yes	Yes

Table 2. Continued

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	State law specific to interchangeability of biologics	Substitution permitted without prescriber approval	Must communicate substitution to the prescriber	Must communicate substitution to the patient
Pennsylvania	Yes	Yes	Yes	Yes
Rhode Island	Yes	Yes	Yes	Yes
South Carolina	Yes	No	Yes	Yes
South Dakota	Yes	Yes	Yes	Yes
Tennessee	Yes	Yes	Yes	Yes
Texas	Yes	Yes	Yes	Not specified
Utah	Yes	Yes	Yes	Yes
Vermont	Yes	Yes[b,c]	Yes	Yes
Virginia	Yes	Yes	No	Yes
Washington	Yes	No	Yes	Yes
West Virginia	Yes	Yes	Yes	Yes
Wisconsin	Yes	Yes	Yes	Yes
Wyoming	Yes	Yes	Yes	Yes

[a]Data are as of July 2021.
[b]Only if at lower cost to the patient.
[c]If requested by the purchaser.

workload in securing prescriptions if payors prefer noninterchangeable adalimumab biosimilars, and confirming the direct telephone or fax numbers of the clinics where the prescriptions originate should be a workflow consideration. Of note, prescribers may indicate "dispense as written" or "brand medically necessary" on a prescription for the adalimumab reference, but, if the preferred product is an adalimumab biosimilar, the reference product is unlikely to be covered by the payor and a new prescription will be needed to dispense the adalimumab biosimilar. Lastly, medication reconciliation in both specialty clinics and pharmacies will be essential to ensure that the correct adalimumab reference or biosimilar product is listed in the patient's medication lists and EHR for accuracy.

As noted in Table 1, adalimumab products will be available in different strengths, volumes, formulations, and administration devices. Pharmacists embedded in specialty clinics and pharmacies are well equipped to provide education about these considerations and ensure that prescribers are comfortable with adalimumab biosimilars. Additionally, pharmacists practicing in specialty pharmacies should review and update their collaborative practice agreements to permit pharmacist autonomy in substituting the preferred agent. A new prescription will be required if the product volume differs between the ordered product and the preferred product, such as when substituting a citrate-free 40 mg/0.8 mL biosimilar for the citrate-free 40 mg/0.4 mL reference product.

Benefits investigation. At present, a new prescription for adalimumab triggers a benefits investigation for the reference product. When the new biosimilar products enter the market, benefits investigation teams will need to clarify (1) whether prior authorization is required and (2) the preferred product according to the plan's formulary. This information is crucial in identifying which product to pursue, assuming that the prescriber is amenable to initiating adalimumab treatment with a biosimilar. To prepare for this, pharmacy staff will require education on the timeline for the launch of new biosimilar products and an overview of these products. Pharmacy staff will also need to be familiar with interchangeability status to ascertain whether a new prescription is needed to pursue access to a preferred agent. If possible, additional resources should be allocated to the department providing benefits investigation services in anticipation of varying biosimilar preferences among payors and various access services provided by the individual manufacturers of biosimilar products.

Switching to a biosimilar from reference adalimumab. For patients currently treated with reference adalimumab, it is expected that some plans may require these patients to transition to an available biosimilar due to the potential for cost savings. In these cases, correspondence between the plan and patient and/or the plan

Figure 1. Checklists for workflow considerations relating to adalimumab biosimilars.

Pharmacies/Specialty Pharmacies

- ☐ Staff education relating to:
  - Adalimumab biosimilar products including formulations considerations and patient resources
  - Interchangeability designation as it pertains to state law
- ☐ Update pharmacy ordering/processing software to ensure product database is up to date
- ☐ Review current support for benefits investigation and prior authorization services and anticipate increased demand/workload
- ☐ If feasible, obtain direct numbers for prescribing provider's office and fax
- ☐ Discussion with payors or trend dispensing to determine which adalimumab products are preferred
- ☐ Order and stock adalimumab reference and biosimilar products with appropriate refrigerator space
- ☐ Start educating patients on reference adalimumab about the potential changes in 2023 to help mitigate nocebo effect
- ☐ For those who transition to adalimumab biosimilar, counsel on potential differences and ensure patients are connected to the correct financial and medication access resources as available per the manufacturer
- ☐ Continue to stay up to date on the adalimumab biosimilar landscape, as more products are lined up for launch and interchangeability laws may evolve
- ☐ Provide monitoring touchpoint at each fill to help mitigate nocebo effect
- ☐ Consider implementing medication safety strategies to prevent errors with dispensing (i.e. tall man lettering, standardized nomenclature for adalimumab products, storage location considerations)

Specialty Clinics (e.g., rheumatology, gastroenterology, dermatology)

- ☐ Staff education relating to:
  - Adalimumab biosimilar products including formulations considerations and patient resources
  - Adalimumab reference and biosimilar products prescription entry and considerations
  - Interchangeability designation as it pertains to state law
- ☐ Update electronic health records to ensure product database for adalimumab biosimilars is up to date
- ☐ Review current support for benefits investigation and prior authorization services and anticipate increased demand/workload
- ☐ If feasible, obtain direct numbers for most commonly utilized specialty pharmacies
- ☐ Discussion with payors or trend dispensing to determine which adalimumab products are preferred among the most common health insurance plans seen in practice
- ☐ Start educating patients on reference adalimumab about the potential changes in 2023 to help mitigate nocebo effect
- ☐ For those who transition to adalimumab biosimilar, counsel on potential differences and ensure patients are connected to the correct financial and medication access resources as available per the manufacturer
- ☐ Continue to stay up to date on the adalimumab biosimilar landscape, as more products are lined up for launch and interchangeability laws may evolve
- ☐ Implement monitoring program post-adalimumab transition to ensure clinical stability and minimize nocebo effect
- ☐ Serve as the primary champion for adalimumab biosimilar and update collaborative scope of practice; continue to refine workflows and be the point person in clinic for patients relating to adalimumab biosimilar education, questions/concerns, and workflow needs

and provider's office should trigger a new benefits investigation to confirm access to adalimumab therapy for each patient. Benefits investigation teams will need to carefully confirm that a new prior authorization is requested by the plan for continuation of reference adalimumab vs switching to a biosimilar. If and when a patient's plan requires switching from reference adalimumab to a biosimilar product, notifying the patient about the need for updated prior authorization is key to streamlining care and minimizing gaps in therapy. Some patients may understandably be concerned about the transition to a biosimilar and request that the insurance mandate be challenged or appealed. Given that transitioning to a biosimilar would be considered appropriate in most clinical situations, pharmacists are well positioned to provide education to patients about biosimilar products and emphasize that appealing such a decision is likely to lead to adalimumab treatment delays, which would be a detrimental course of action, as opposed to switching to a biosimilar and continuing treatment without any interruptions. Additionally, pharmacists need to consider the financial implications of switching adalimumab products and ensure that the affordability of the biosimilar is secured via a copay savings program or patient assistance program.

Similarly, given the launch of several adalimumab biosimilar products on the market, it is possible that payors may update their formularies, subjecting patients to multiple switches to adalimumab biosimilars. Emerging data have shown no worsening of clinical outcomes or adverse effects when switching from one adalimumab product to another, but data evaluating switching among 3 or more adalimumab biosimilars are currently lacking.[39] Pharmacists are well positioned to stay up to date on emerging literature and provide education on such data once they are available.

Affordability. Biosimilars are designed to stimulate market competition and lead to lower healthcare costs due to their lower list prices compared to their reference biologic products. Unfortunately, these cost savings may not extend to the patient level depending on the insurance copay structure or the availability of patient financial assistance programs. If a plan requires a patient to initiate or transition to an adalimumab biosimilar and an authorization for the product has been secured, the patient should be directed to the specific manufacturer of that product for financial support and resources. Pharmacists are well positioned to help patients navigate this landscape, and, if this opportunity is missed, patients may end up paying more in copays than if they were on the reference product.

Currently, a copay card is available for reference adalimumab with a robust amount of funding and patient assistance programs for uninsured or underinsured patients and those with Medicare. Potential financial considerations with the adalimumab biosimilars include a lack of patient assistance programs inclusive of Medicare patients with unaffordable copays and off-label dosing (beyond the maintenance regimen of 40 mg every 14 days). The manufacturer of reference adalimumab currently offers additional resources such as nursing

assistance with injection training and easy product replacement in the setting of device malfunction or misfire, and it is unclear whether the manufacturers of adalimumab biosimilars will offer the same programs. Pharmacists should become familiar with the financial and patient access resources that are available for each biosimilar product.

Provider education. Given the considerations relating to adalimumab prescribing and use highlighted above, providers (including residents and fellows) will likely need education on the concepts of biosimilarity and interchangeability, as well as an overview of the anticipated adalimumab products and their features. Pharmacists within the health system and/or specialty pharmacies servicing patients receiving care from specialty clinics are well positioned to provide in-services on adalimumab biosimilar products and tips and tricks on navigating this landscape for patients currently stable on or initiating treatment with adalimumab. For example, a common concern among providers relates to biosimilar efficacy and safety. Pharmacists can help address these concerns by reviewing the currently available data demonstrating that biosimilars have similar efficacy without increased risk of immunogenicity.[40] Pharmacists working under collaborative practice agreements will need to update these documents to include biosimilar products and allow for substitution with noninterchangeable biosimilar products preferred by payors; during this process, they can also help establish workflow-related protocols as permitted. Lastly, clinic support staff involved in prescription entry and/or maintenance will likely also need education on the nuances of switching to or initiating an adalimumab biosimilar product, as all clinic staff should be comfortable with and confident in the adoption of these new agents.

Patient education. A primary role of clinical pharmacists practicing within specialty clinics and pharmacies is patient education regarding specialty medications, including dosing, administration, adverse drug reactions (ADRs), and stability at room temperature. Although most counseling points will apply to both adalimumab reference and biosimilar products, pharmacists should be aware of the differences and tailor the counseling approach accordingly. Utilization of motivational interviewing will also be essential, particularly if patients are uncomfortable with switching to or administering an adalimumab biosimilar, as there may be variations in the formulation.

Treatment and safety evaluation. Biosimilars produce the same therapeutic effect and carry similar risks for ADRs as the reference product. However, patients may experience new ADRs or report a different level of satisfaction with biosimilar treatment given variations in the listed excipients and needle gauges. Given their longitudinal follow-up with patients, pharmacists are well positioned to identify variations in clinical response, assess ADRs, and evaluate for potential nonadherence with the biosimilar product. In the specialty clinic, pharmacists may also assist with immunogenicity evaluations as clinically appropriate. Although no acute changes in disease control and tolerability are expected, patients may experience ADRs or symptoms in the context of the nocebo effect, which occurs when patients have negative expectations about biosimilars and is not due to the treatment itself.[41] To help mitigate the nocebo effect, pharmacists should offer closer follow-up or appointments to monitor patients after they switch and provide reassurance as needed.

Specialty pharmacy business and dispensing considerations. Pharmacy leadership should review all pharmacy contracts for adalimumab and biosimilars as early as possible and negotiate favorable terms for their pharmacies and patients. Although the lower list prices of biosimilars should lead to healthcare savings, pharmacies may be reimbursed less than their acquisition cost due to supply chain incentives. Additionally, specialty pharmacies with the opportunity to acquire specialty medications at a reduced cost due to 340B Drug Pricing Program eligibility may ensue reduced margins with the adalimumab biosimilars. Key stakeholders who oversee the pharmacy's business plan and/or budget should consider the lower net revenue for patients initiating or continuing therapy with a biosimilar. Careful review of pharmacy contract pricing and creating financial models to estimate net revenue will help guide business planning decisions. The goal is to support a competitive market where biosimilars lead to lower costs for the pharmacy and patients.

All specialty pharmacy leadership should be aware of adalimumab biosimilars and start preparing for potential increased staffing and overhead costs associated with expanding inventory to include multiple adalimumab products. Confirmation with inventory leaders is necessary to guarantee successful procurement of adalimumab biosimilars. Given the emergence of several adalimumab biosimilars and more in the pipeline, specialty pharmacies may be required to stock all of these products, generating increased inventory costs. It should also be noted that physical space will be needed to store an additional adalimumab product in a temperature-monitored refrigerator, and, to maximize medication safety, each adalimumab product should be stored separately and labeled with tall man lettering. One potential strategy to help mitigate unnecessary overhead costs is to identify the demand for certain products, as this is likely to be payor driven. Although unlikely, biosimilar manufacturers may limit distribution to certain wholesalers, which would impact a specialty pharmacy's ability to provide medication to patients who are restricted to certain products by their insurance.

Specialty pharmacies may hold multiple licensures to service patients residing in states beyond the physical location of the pharmacy. Given that biosimilar interchangeability varies by state with regard to whether

automatic substitution is permitted and how/when patients and providers should be notified if such a substitution occurs, pharmacists working in multistate-licensed facilities should be aware of these considerations and dispense adalimumab biosimilar products accordingly.

Outcomes evaluation and quality improvement

Pharmacists will have an important role in evaluating and disseminating the real-world impact of adalimumab biosimilars on clinical, economic, and humanistic outcomes. Planning for evaluation should be multidisciplinary and include patients, pharmacists, providers, and other stakeholders. Pharmacists could evaluate clinical outcomes before and after the transition to biosimilars, patient and provider satisfaction with biosimilars and the education provided by pharmacists, patient perceptions of the ease of use of biosimilars, safety outcomes, impact on pharmacy operations and workflows, cost to the pharmacy and patients, availability of patient financial assistance, and financial outcomes. Specialty pharmacies should consider including biosimilar implementation in their quality improvement plan, thus providing an opportunity for continuous evaluation and improvement of processes as this rapidly changing market evolves. Both pharmacists and specialty pharmacies have an opportunity to help shape the growing biosimilar market through quality improvement, research, and dissemination of outcomes.

Conclusion

This year and beyond will bring many changes to the specialty pharmacy landscape, with the introduction of several adalimumab biosimilar products, formulary changes, and interchangeability, permitting pharmacists to participate in automatic substitutions depending on state pharmacy laws. These changes will greatly impact pharmacists working in specialty clinics or pharmacies, and pharmacists will be considered an essential stakeholder, given that they are positioned at the forefront and will be easily accessible to many patients during this period of changes. Herein we have outlined important considerations pertaining to adalimumab biosimilars and provided checklists for workflow modifications to prepare pharmacists for these exciting times ahead.

Disclosures

Dr. Cisek has served on the advisory board for AbbVie and is a consultant for Boehringer Ingelheim and Fresenius Kabi. Dr. Choi has served on the speaker bureau for Janssen Pharmaceuticals and has served as a consultant to Bristol Myers Squibb, Prometheus Laboratories, Boehringer Ingelheim, AbbVie, and Janssen Pharmaceuticals. Dr. Bhat has served on the advisory board for Bristol Myers Squibb, Prometheus Laboratories, Boehringer Ingelheim, and Pfizer and is a consultant for AbbVie.

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