PHARMACIST CE:

Pharmacist's Role in Demystifying the Fears of Biosimilar Humira® Use in Rheumatology

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Rheumatic diseases and their related conditions create a significant burden on the US healthcare system, as approximately 1.3 million adults live with rheumatoid arthritis or other rheumatic illnesses.[1] Biologics have an expansive role in the treatment of rheumatic diseases, paving the way for their respective biosimilars. Fifty-two percent of patients with RA use a biologic, with an estimated annual cost of $36 billion dollars.[2,3] Compared to conventional, small-molecule drugs, biologics or biological products are larger and more complex preparations derived from living organisms, including animal cells, human cells, and microorganisms.[3] These products are composed of a single entity or a combination of proteins, carbohydrates, and nucleic acids, among other constituents.[4] Examples of currently marketed biologics include monoclonal antibodies, therapeutic proteins, and vaccines. These Food and Drug Administration-regulated products have many therapeutic indications that target a wide range of medical conditions, such as RA, diabetes, and multiple sclerosis.[4]

CE FOR **PHARMACISTS**

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Learning Objectives

- Recognize the current climate and trend of biosimilar use in rheumatology
- Acknowledge various challenges delaying the adoption of biological products
- Describe the FDA regulatory pathway for biosimilars and the impact of patents on patient care
- List various strategies used to support biosimilar uptake
- Articulate the relevance of biosimilar use to practicing pharmacists
- Recognize how pharmacists in different practice settings can be leveraged to improve biosimilar accessibility

Abstract

Rheumatic diseases are prevalent in the United States, and the number of patients with rheumatic conditions is only expected to grow. Biological therapies play an extensive role in the treatment of these diseases, paving the way for the use of associated biosimilars. Several barriers persist and prevent effective use of biosimilars for these conditions. Patient and provider perception, confusion surrounding nomenclature, and the inherent complexity of biosimilar development all present challenges to the incorporation of biosimilars in rheumatology. With these barriers in mind, pharmacists play a vital role in expanding biosimilar use, from those practicing at the community level to those representing the pharmaceutical industry. Where biosimilars are concerned, pharmacists can help improve patient care and quality of life for patients, as well as help increase medication access and reduce costs.

ACA - Affordable Care Act
ACR - American College of Rheumatology
AS - Ankylosing spondylitis
AWP - Actual wholesale price
BLA - Biologic license application
BPCIA - Biologics Price Competition and Innovation Act
CE - Continuing education
CPOE - Computerized prescriber order entry
EMR - Electronic medical record
FDA - Food and Drug Administration
HCP - Health care providers
IBM - International Business Machines
KOL - Key opinion leader
mAb - Monoclonal antibody
MPR - Medication possession ratio
MS - Multiple sclerosis
P&T - Pharmacy and therapeutics
PBM - Pharmacy benefits manager
PDC - Proportion of days covered
PsA - Psoriatic arthritis
PSP - Patient support program
RA - Rheumatoid arthritis
RAPID3 - Routine assessment of patient index data 3
RCT - Randomized controlled trial
TNF-α - Tumor necrosis factor-alpha
US - United States
VAS - Visual analog scale

Similarities and Differences between Brand-Generics and Biologics-Biosimilars

Conceptually, the relationships between brand-name and generic medications and those between biologics and biosimilars are very much alike. For instance, the initiation of commercialization for biosimilars and generics depends on the expiration of brand-name medications' patents and market exclusivity. Like their brand-named counterparts, biologics serve as a reference or originator product for biosimilars. However, unlike small-molecule drugs where the brand and generics have identical chemical structures, a biosimilar only highly resembles its reference biological product, due to its size and complexity. Additionally, as part of the enactment of the Affordable Care Act, the FDA was granted authority to license biosimilars via the biologics license application (BLA).[1] Under this legislation, the biosimilar sponsor has access to the preclinical and clinical data of biologics, permitting an abbreviated approval process for biosimilars.[5] Following approval, the FDA performs post-marketing surveillance of all biological products to ensure safety and efficacy in clinical use.[3,5] Nonetheless, the differences between biosimilars and the FDA-approved reference product are not considered clinically significant.[5] The currently approved biosimilars are listed in Table 1.

Biosimilars and Increased Patient Access to Disease-Modifying and Lifesaving Medication in Rheumatology

Cost is a major barrier to implementing biological medications for the treatment of complex disease states; these products are difficult to manufacture, less durable than small molecule drugs, and often require special storage conditions. It can be difficult to recommend biological agents as first-line treatment for a disease such as RA because of the cost. The total overall cost of RA medications in April 2018 was estimated at $20 billion dollars, and it was predicted during a review that it would reach $36 billion dollars by 2021.[6] Infliximab biosimilars have been available since 2013, allowing considerable price discounts for patients in some regions.[7] These discounts proposed by the biosimilar manufacturer increase access to medications that could have substantial positive effects on patients' quality of life. Since biosimilars do not require clinical trials for FDA approval, manufacturers can lower the actual wholesale price of the drug by excluding the cost of the trials, thus increasing the affordability of the drug.[5] For example, a reference product, Remicade® (infliximab), had an AWP of $1,401.38 per 100-mg vial in September of 2020.[5] This price can be compared to three biosimilars on the market, where during the same time period, the cost of Inflectra® was $1,135.54, Renflexis® was $904.07, and Avsola® was $600.[5] Another factor facilitating increased patient access to biological products is insurance formulary preference. This is driven by the lower costs of biosimilars; therefore, insurance companies prefer to cover biosimilars as opposed to the more expensive biologics on their formulary. It is important to understand that biosimilars offer greater affordability without giving up therapeutic performance to reference product biologics, and the discounted rate can make a meaningful impact to patients.

Humira and its Biosimilars

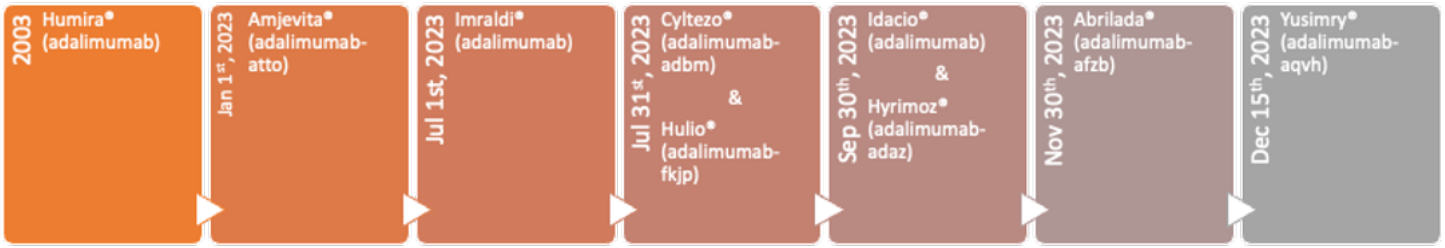
Adalimumab (Humira®) is a prime example of a biological product that demonstrates how the cost-effectiveness of biosimilars can increase patient accessibility. This marketed biological product has altered the treatment course of many debilitating diseases, including RA, Crohn's disease, and psoriasis.[2] Moreover, Humira® is a top-selling medication globally.[8] The medication dominates the market, having more than double the number of sales of the second highest-selling medication in 2018.[9] AbbVie generated $19 billion in global sales from Humira® (adalimumab) in 2019, of which $15 billion came from the US alone.[8] With that said, AbbVie currently faces the challenge that all drug manufacturers fear in an expiring patent. This threat to the

TABLE 1. Current Rheumatologic Biologic and Biosimilar Therapies

Biologic (brand name)	*Drug class*	*Indications*	*Approved biosimilars*
Adalimumab (Humira)	TNF-a inhibitor	Ankylosing spondylitis, Crohn's disease, hidradenitis suppurativa, psoriasis, rheumatoid arthritis, ulcerative colitis, and uveitis	Abrilada (adalimumab-afzb) Amjevita (adalimumab-atto) Cyltezo (adalimumab-adbm) Hadlima (adalimumab-bwwd) Hulio (adalimumab-fkjp) Hyrimoz (adalimumab-adaz) Yusimry (adalimumab-aqvh)
Etanercept (Enbrel)	TNF-a inhibitor	Ankylosing spondylitis, graft-vs-host disease, psoriasis, and rheumatoid arthritis	Erelzi (etanercept-szzs) Eticovo (etanercept-ykro)
Infliximab (Remicade)	TNF-a inhibitor	Ankylosing spondylitis, Crohn's disease, psoriasis, rheumatoid arthritis, sarcoidosis, and ulcerative colitis	Avsola (infliximab-axxq) Inflectra (infliximab-dyyb) Ixifi (infliximab-qbtx)A Renflexis (infliximab
Rituximab (Rituxan)	CD20+ B-cell inhibitors	Non-Hodgkin's Lymphoma, Chronic Lymphocytic Leukemia, lupus nephritis, and rheumatoid arthritis (not an exhaustive list)	Riabni (rituximab-arrx) Ruxience (rituximab-pvvr) Truxima (rituximab-abbs)

At the time of this writing, there are four biologics indicated for rheumatological diseases each with their accompanying biosimilars.[5] Biosimilars for infliximab and rituximab are currently available, while adalimumab and etanercept biosimilars are expected to come to market within the next five years.[1] As the development of biosimilars continues to grow and treatment options expand, pharmacists must stay up to date to support patients' access to these traditionally expensive medications.

FIGURE 1. Anticipated Release Dates of Humira® and its Biosimilars in the U.S.



Timeline of Humira® release date, along with the approval and planned release dates of its accompanying biosimilars. Adopted from Coghlan J et al.

company's profit margin is an opportunity for the entry of competitors in the form of biosimilars, which is bound to reinstate cost control of this medication on the market. In a study conducted by Lee and colleagues in 2021, Medicare could have saved $2.19 billion on reported adalimumab spending if there had been a biosimilar alternative after accounting for rebates between 2016 and 2019.[8]

When focusing on the patient cost of biologics, a study performed by the American College of Rheumatology (ACR) suggests that although most people with rheumatic ailments have insurance, six out of ten patients struggle to pay for their medications.[10] The study revealed that patients are burdened by expensive biologics due to their market monopoly. Considering the economic strain on patients, the federal health programs, and health systems alike, it further highlights the need for pharmacists to be invested in improving biosimilar uptake and patient access to these life-altering medications.[8]

The FDA has already approved seven biosimilars to adalimumab; however, they will not be launched until 2023 due to patent disputes with AbbVie (Figure 1).[9] Timely marketing of new biosimilars will be crucial to ensuring that the US healthcare system has more treatment options and cost savings available for patients.[8] With the imminent patent expiration in 2023, the impact of biosimilars on market cost, patient accessibility, treatment course of numerous diseases, and overall market equilibrium is highly anticipated.

Current and Potential Challenges to Incorporating Adalimumab Biosimilars into Rheumatology Practice

Some of the current challenges to biosimilar uptake in rheumatology are patient nocebo effects, payor reimbursement issues, negative patient perception, confusion surrounding naming and labeling, lack of confidence in its use of extrapolated indications, and prescribers' fear of crossover immunogenicity and subpar efficacy.[11] The nocebo effect can be defined as a patient's negative expectation of treatment that leads to suboptimal efficacy unrelated to the physiological effect of the medication.[12] This negative perception is clear in Frantzen et al's French nationwide survey on 629 patients' perceptions of biosimilars.[13] The team found that patients were reluctant to switch to biosimilars even if it was required by their disease state.[13] Addressing this nocebo issue is important, because it has the potential to give the patient or provider a false perception that biosimilars are inferior. The problem associated with payor reimbursement is evident in some insurance profit-oriented practices, such as the use of a single-source mandate to prevent coverage of specific biosimilars. For instance, Chambers and colleagues revealed that only 14% of biosimilars were granted preferred coverage out of 535 decisions issued by plans.[14] Alternatively, originator manufacturers may use existing price rebates as an incentive to prevent insurance companies and pharmacy benefit managers (PBM) from adding biosimilars to their formulary.[10]

Another barrier to biosimilar uptake is the complexity of nomenclature. Regulatory requirements mandate the inclusion of the four unique, clinically insignificant suffixes added at the end of the originators' and the biosimilars' statement: "BIOSIMILAR-xxxx is a biosimilar to ORIGINATOR," followed by a disclosure indicating that the two medications are highly similar with no clinically meaningful differences.[7] The suffix and the biosimilar statement are often misinterpreted as evidence of inferiority by both health care providers and patients alike.[4] The fear of subpar efficacy along with crossover immunogenicity are major barriers to biosimilar uptake, as it prevents providers from prescribing biosimilars in the first place.[15] Furthermore, providers and patients lack confidence in using biosimilars for extrapolated rheumatic indications. Extrapolation of indication refers to the process whereby an approved biosimilar can use the originator's licensed indications with some limitations. These extrapolated indications have not been studied in a head-to-head clinical trial by biosimilar manufacturers.[15]

The Role of Pharmacists in Increasing Biosimilar Uptake in Rheumatology

Why Should Pharmacists Care about Increasing Adalimumab Biosimilar Use?

As 2023 fast approaches, at least eight biosimilars of the blockbuster drug Humira® (adalimumab) will be licensed and launched on the US market.[16] Hence, it is essential for stakeholders to strategize how to maximize the cost reduction associated with the biosimilar influx. It is well established that pharmacists are medication experts, so the onus is on the profession to ensure a smooth transition to implementing these complicated yet cost-saving medications. Although the introduction of these biosimilars is good news for patients and health systems alike, it will be an uphill battle because of the inevitable barriers posed by their entry to the market.

Proof of effective pharmacist intervention is another reason for pharmacists to be invested in increasing biosimilar uptake. A cross-sectional study was performed to assess information

and concerns among French patients treated with biosimilars for rheumatic inflammatory disease.[13] This study performed a multivariate analysis of 629 participants, and they found that adequate information was the independent factor associated with reduced fear of biosimilar use in patients.[13] The evidence supports that patient education, a strong domain of pharmacists, helps improve user perception of biosimilars.

How can Pharmacists from Various Practice Sites Unite to Increase Adalimumab Biosimilar Uptake?

Pharmacists are poised to be educators for other health care providers (HCPs), patients, and caregivers about these innovative adalimumab biosimilars across various practice sites (Figure 2). The goal of this educational campaign would be to promote the uptake of adalimumab and other biosimilars in treating rheumatic and other diseases.[17] Biosimilar education should focus on reviewing safety, efficacy, immunogenicity, and extrapolation from clinical studies.[17]

In a national survey aimed at understanding potential barriers to biosimilar use, 86% of providers identified education on evidence of switching studies and post-marketing data as a challenge.[18] Hence, targeting provider education would increase the likelihood that these cost-saving medications would be prescribed, and combat patient reluctance of switching to biosimilars.[13] As shown by the French Rheumatology Association, rheumatologists are uniquely positioned to predict if a patient is a good candidate for a biosimilar switch. This prediction can be made using the available clinical, efficacy, and economic data. Additionally, the rheumatologist's influence over a patient's decision to switch to biosimilar is evident in a survey reporting that 79% of 629 patients trust their rheumatologists as reliable information outlets.[13] To address this barrier, pharmacists can create biosimilar educational materials, policy, tool kits, etc. that educate patients and/or providers and may serve as continual education (CE) credits for HCPs.[17] A united effort in the pharmacy community will pay dividends by increasing the confidence and use of these biosimilars and combat the traditionally slow uptake to new formulations.[17,19]

FIGURE 2. Pharmacist's Role in Improving Access to Biosimilars in Various Practice Settings

Figure 2: A breakdown of different pharmaceutical practice sites, and their respective roles in improving biosimilar access

Furthermore, pharmacists can address the patients' and providers' lack of confidence with extrapolated indications. Frantzen et al discovered that 88 of every 100 patients of 629 respondents were not content with the principle of the indication extrapolation.[13] In a survey of 246 respondents, 48.5% of prescribers reported they will likely delay incorporating these biosimilars into practice until post-marketing data supports their efficacy in therapy.[20]

Given the patient and provider apprehension with extrapolated indications, the goal for the pharmacy community is to normalize the scientific principle behind extrapolated indication. This may be achieved by reminding prescribers, patients, and other stakeholders through various platforms that the extrapolation principle has been widely used for decades.[21] This extrapolation approach is often preferred by manufacturers because it does not require them to repeat costly and time-consuming clinical trials to ensure the safety and efficacy of the approved medication after a non-clinically relevant update to the medication or its manufacturing process.[22] Although these updates may alter the biologics from the initially approved formulation and structure, the changes are not clinically significant, and the medications are, nonetheless, still efficacious in the preapproved indications.[22] Additionally, the NOR-SWITCH study, a double-blinded, randomized non-inferiority phase IV trial, demonstrated the efficacy and safety of an infliximab biosimilar across an array of diseases compared to its originator.[22] Sharing medical literature and current biological manufacturing process may help ease the providers' reservations about using biosimilars for extrapolated indications.

Role of Specialty Pharmacists

Specialty pharmacists have an important role in increasing biosimilar use in rheumatology. These pharmacists assist in the delivery of these complex and expensive medications to patients by handling the maintenance of the cold chain distribution and dispensing biosimilars. Specialty pharmacists also play a key role in negotiating payors' contracts and ensuring patient safety and medication efficacy.[23] Hence, specialty pharmacists are well positioned to address the following issues:

- Nocebo effect associated with biosimilar switch
- Complex biosimilar switching process
- Monitoring of patient's adherence and medication efficacy
- Use of databases for pharmacovigilance and clinical efficacy monitoring

For instance, specialty pharmacists can address the nocebo effect by showing confidence and using positive language when communicating with patients before the switch to a biosimilar happens.[12]

TABLE 2. Randomized Controlled Trials (RCTs) and Open Label Extension Switch Studies

Authors	Product	Population	Study Design	Number Patients Switched	Follow-up	Efficacy, Safety, and Immunogenicity Outcomes	Conclusion
Cohen et al. (2017)[27]	Adalimumab – ABP 501	RA	Open-label extension study of a Phase III trial • Switch arm: change from adalimumab to ABP501 • Continue arm: stay on ABP501	237	46 weeks	• Similar percentages of subjects reaching ACR20 (specific numbers not provided) • Similar rates of TEAE (switch: 65.0%, continue: 62.4%, no statistics provided) • Similar percentages of subjects developing neutralizing antibodies at any time between two arms (switch: 13.9%, continue: 14.4%, no statistics provided)	Long-term safety, immunogenicity, and efficacy results were comparable between switch and continuing arms
Cohen et al. (2018)[28]	Adalimumab – BI695501	RA	Randomized double-blind, parallel arm, phase III trial (VOLTAIRE-RA)	147	34 weeks	• Percentages of patients with good response per EULAR grading between RP continued and switch were 35% and 31%, respectively. • Percentages of patients with moderate response per EULAR grading between RP continued and switch were 47% and 52%, respectively. • Percentages of patients with at least 1 drug-related AE between RP continued and switch were 22.9%, and 19.2%, respectively. • Immunogenicity was similar across arms (no statistics provided)	The switch had no impact on efficacy, safety, and immunogenicity
Hodge et al. (2017)[26]	Adalimumab – CHS-1420	PsO and PsA	Double-blind, randomized, parallel arm, phase III trial	124	8 weeks	PASI75 achieved in 84.6%, 81.6%, and 88.3% of patients in BS continued, switch, and RP continued arms. TEAE reported in 20.1%, 19.4%, and 16.3% pts in BS continued, switch, and RP continued arms.	Similar safety and efficacy between switched and nonswitched pts
Papp et al. (2017)[29]	Adalimumab – ABP 501	Ps	Randomized, double-blind, parallel arm, phase III trial	77	36 weeks	• No significant differences across arms in percentages of PASI50/75/90/100 at week 50 (RP continued: 94.3%/87.1%/64.3%/35.7%, and switch: 92.8%/81.2% /66.7%/34.8%) • Percentages of TEAE between RP continued and switch were 65.8%, and 70.1%, respectively. • Percentages of patients with binding antibodies at any time were comparable across arms (RP continued 74.4% and switch 72.7%)	Similar efficacy, safety, and immunogenicity profiles after single switch between arms
Weinblatt et al. (2018)[30]	Adalimumab – SB5	RA	Extension. Double-blind, randomized, controlled phase III trial	125	28 weeks	• ACR20/50/70 response rates at week 52 for the RP continued and switch arms were 73.4%/50.8%/28.2% and 78.8%/54.2%/26.3%, respectively. • AE rates for the RP continued and switch arms were 37.6% and 33.1%, respectively. • Incidence of overall antidrug antibodies for the RP continued and switch arms were 18.3% and 16.8%, respectively.	Switching had no treatment-emergent issues, such as increased AEs, increased immunogenicity, or loss of efficacy

ACR20: American College of Rheumatology; ADA: anti-drug antibodies; AE: adverse event; BS: biosimilar; EUCLAR: European Alliance of Associations for Rheumatology; PASI: Psoriasis Area and Severity Index; PsO: plaque psoriasis; PsA: psoriatic arthritis; RA: rheumatoid arthritis; RP: reference product; TEAE: treatment-emergent adverse event. Reported data and concluding remarks from randomized controlled trials (RCTs) and open label extension switch studies for Humira

Moreover, these pharmacists can help ensure that all HCPs on the patient's care team have consistent positive messaging about adalimumab biosimilars; a united front will potentially present the patients with less anxiety, skepticism, and confusion about the biosimilar.[12] Specialty pharmacists can also simplify the biosimilar switching process by creating a before-switching checklist.[12] This checklist would contain reminders and a timeline of crucial administrative tasks needed for a smooth transition by using a new patient support program (PSP).[12] These types of programs help improve access, usage, and adherence to patients' new medications.

Additionally, pharmacists can increase biosimilar uptake by addressing HCPs' reluctance to use biosimilars due to fear of cross immunogenicity and inferior efficacy.[15] The provider's reluctance to prescribe biosimilars to biologic naïve patients is evident in Gibofsky and McCabe's survey on the beliefs of US-based rheumatologists about biosimilars. The findings suggest that rheumatologists are reluctant to switch especially when patients are doing well.[24] Studies like the PLANETRA trial, a double-blind, randomized, multicenter, multinational prospective study with parallel group, found that there were no signals to suggest switching to biosimilars of infliximab caused increased anti-drug or neutralizing anti-drug antibodies.[22,25] Pharmacists can use the studies described in Table 2 to compile evidence-based answers and recommendations, which can assuage fears associated with biosimilar use. Ultimately, this can help to improve the providers' confidence in prescribing biosimilars to both originator naïve and non-naïve patients.[24]

Furthermore, specialty pharmacists can help monitor patients' adherence and medication efficacy. This can be accomplished by ensuring that billing data is reconciled with the patient's insurance claims and using the medication possession ratio (MPR) and proportion of days covered (PDC) to calculate a patient's adherence rates.[31] Specialty pharmacists can also monitor the biosimilars' longitudinal safety and efficacy profiles by using tools like the Visual Analogue Scale (VAS) to assess fatigue, pain, and quality of life, and the routine assessment of patient index data 3 (RAPID3) or Likert scale to optimize patient-oriented outcomes.[12]

TABLE 3. Proposed Tactics to Overcome Barriers to Biosimilar Adoption Towards Achieving BPCIA Goals, Adapted from Edgar et al.[18]

Biologic (brand name)	*Approved biosimilars*
Educational program about biosimilars	• Organize multi-stakeholder educational programs involving payers, providers, and patients » Provide education focused on biosimilar safety and efficacy, interchangeability, switching studies, and real-world evidence from post-marketing studies » Involve pharmacists in leading education on biosimilars » Leverage educational formats that facilitate peer-to-peer and team-based discussion of evidence and applications, such as grand rounds, small group sessions, and programs in specialty departments » Tailor education to providers in the community
Administrative processes for biosimilars	• Streamline prior authorization requirements to improve patient access to biosimilars and promote rapid reimbursement to providers who prescribe biosimilars • Increase communication with providers about biosimilar coverage criteria and cost savings from switching to biosimilars
Financial incentives	• Contribute to initiatives attempting to reduce cost sharing to patients receiving biosimilar and increase provider reimbursement for biosimilars through fee schedule adjustments • Relate the cost savings realized from switching to tangible benefits to providers » Benefits to physician practices may include hiring experienced staff or pharmacists or other investments

Tactics proposed to overcome obstacles preventing biosimilars from reaching goals set by the BPCIA.[13]

Additionally, because specialty pharmacists have access to real-world data, they can facilitate the design and maintenance of nationwide databases for biosimilar safety and efficacy. This can be done in collaboration with other pharmacists to ensure the optimal design and maintenance of a robust pharmacovigilance program.[18] The information and trends received from these databases can also serve as clinical evidence to provide information about the safety and efficacy of biosimilars to rheumatologists, other providers, and the public.[18,22]

Role of Informatics Pharmacists

The naming requirements for biosimilars are also considered a barrier to biosimilar uptake in rheumatology.[11,18,22,23] The required four-letter suffixes have been a source of concern for multiple stakeholders because they are often misperceived by both HCPs and patients as having a clinically meaningful difference.[23] At first glance, these suffixes might seem like an unnecessary logistical quagmire. As evident in the Kolbe et al US national survey of the understanding and willingness of physicians to prescribe biosimilars, 46% of the 507 specialty physicians thought that these suffixes were cumbersome.[20] However, these suffixes are especially important because adequate naming is a crucial part of any pharmacovigilance and adverse event reporting program, as well as billing and ordering in electronic medical records.[20]

Clinical informatics pharmacists are experts at using electronic health data to support the safe and effective use of medications. They are poised to aid in the simplification and demystification of the logistical issues surrounding the incorporation of these naming conventions into the electronic medical records, e-prescribing, computerized prescriber order entry (CPOE), and electronic medical records (EMR).[32] Additionally, informatics pharmacists can also aid in streamlining the prior authorization approval process in the EMR.[33] Furthermore, they can help integrate biosimilars into the rheumatology treatment pathways, protocols for switching and interchangeability, as well as listing the appropriate extrapolated indications.[19] As a result, informatics pharmacists can help simplify the biosimilar prescribing process, thereby reducing the reluctance of providers to prescribe biosimilars in rheumatic conditions, and by extension other disease

states.

Role of Community Pharmacists

Community pharmacists are known to be some of the most accessible health care professionals.[34] A cross-sectional study using International Business Machines (IBM) MarketScan claims data to compare rates of visits done by pharmacies and physicians (or other qualified health care professionals), found that beneficiaries visited the community pharmacy 1.5-2 times more often than they visited their physicians and qualified health care providers.[34] Due to the easy accessibility and high volume of community pharmacists, these front-line professionals must have a general understanding of biosimilars and rheumatology to assuage patients' fears and misconceptions about these life-preserving medications.[35] In addition, community or independent pharmacists can increase their revenue streams by creating biosimilar seminars or webinar services tailored to patient advocacy groups, such as rheumatology support groups.[21] Independent pharmacies in rural areas can create biosimilar medication services by partnering with specialty pharmacies and health systems to provide biosimilars to patients in rural areas. These services can include medication delivery to ensure the integrity of the cold chain, hosting video telehealth biosimilar medication monitoring visits, parenteral biosimilar administration, etc. These services will not only increase their revenue streams but can also ensure the optimal efficacy of these biosimilars through the maintenance of the cold chain distribution.

Role of Health System Pharmacists

Pharmacists working in a hospital or health system setting have an important role in improving biosimilar access in clinical practice given their interactions with several key stakeholders in the medication supply chain. At the health system level, pharmacists can promote the adoption of biosimilars into the formulary by using their clinical knowledge and extensive training in pharmacoeconomic and pharmacotherapy to highlight the benefits and cost-effectiveness of biosimilar adoption. The cost-effectiveness evidence collected and analyzed by a health system pharmacist should be shared not only with the health system's management but also with the pharmacy and therapeutics (P&T) committees, as well as contracting with insurance companies and other third-party payers.[33] As biosimilars are adopted into the formulary, health system pharmacists can further promote their clinical use by coordinating with other providers to develop evidence-based guidelines, emphasizing how providers can integrate biosimilars into daily practice while protecting patient safety and medication efficacy. Other strategies that could be initiated by pharmacists to promote biosimilar adoption are demonstrated in Table 3.[18]

Role of Managed Care Pharmacists

Cost is a major barrier to medication access in the category, especially specialty medications. Therefore, pharmacists working in a managed care setting are key in tackling hesitancy in biosimilar adoption, since they can directly influence the transition from biologics to biosimilars. To promote biosimilar adoption, pharmacists working at PBMs should be involved in negotiating with manufacturers to obtain the most cost-effective biosimilars for their patient populations and simplifying prior authorization and other administrative barriers that can delay or impede biosimilar uptake by providers.[17] Additionally, pharmacists can significantly alter how biosimilars are used via formulary management. Similarly, drug information pharmacists at PBMs can conduct comprehensive literature evaluation, analyze real-world evidence, and develop a favorable cost containment structure in favor of biosimilar uptake.[17] All these strategies will incentivize payers, providers, and patients to switch to or start with a biosimilar for certain disorders.

Role of Industry Pharmacists

Industry pharmacists are integrated into the drug development process and thus are well positioned to support biosimilar uptake. Pharmacists working in the clinical development and pharmacovigilance functional areas can support their organizations by ensuring that proper clinical trials are performed post-FDA approval to demonstrate the non-inferiority and immunogenicity safety profiles of biosimilars.[17] Regulatory affairs pharmacists have a strong background in literature evaluation and biopharmaceuticals and can take the lead in overlooking the biosimilar application review process.[17] Furthermore, medical affairs pharmacists can leverage their information dissemination machinery to communicate directly with key opinion leaders (KOL) to influence biosimilar uptake.

Conclusion

The exponential growth of biologics as disease-modifying agents in rheumatology presents new challenges to patients and the overall healthcare system. To combat rising costs without sacrificing the improved quality of life brought forth by biologics, the most logical solution is to use biosimilars. This is not a novel idea, as seen in its implementation in oncology medications; however, its use in rheumatology is minimal at best.[15] Evidence shows that pharmacists can be very impactful in improving biosimilar uptake through education of pertinent stakeholders, streamlining the prior authorization process, and demystifying misconceptions surrounding the suffixes attached to biosimilars, and the notion that biosimilars can cause increased immunogenic reactions.[11,36,37] It is important to note that there are limitations to what pharmacists can do to increase biosimilar use. Unlike generic substitution, pharmacists cannot directly substitute biosimilars for originators at the point of sale unless the biosimilar is an interchangeable product. The good news is that the FDA has approved Cyeltzo (adalimumab-adbm) as an interchangeable biosimilar for Humira®. But until policies surrounding biosimilars are changed, HCPs must work together to allay the fears and refute the misconceptions surrounding biosimilar use. For adalimumab biosimilars that will be released in 2023 and beyond, pharmacists must encourage other HCPs, patient advocacy groups, and government officials to become passionate and ardent advocates of biosimilars. This pharmacist-coordinated, multipronged approach will culminate in assuaging fears associated with the integration of these medications.

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Assessment Questions

1. **True or False**: While there are no FDA-approved biosimilars currently used in rheumatology, their use is expected to rise in the coming years.
   a. True
   b. False

2. In what way do biosimilars differ from generic medications?
   a. They don't; biosimilars are identical to generics.
   b. Generic medications demonstrate identical chemical structures to their branded counterpart, while biosimilars have more variability.
   c. Unlike generics, biosimilars can be marketed before the patent of the branded medication has expired.
   d. The differences between biosimilars and biologics can be clinically significant

3. **True or False**: Health system pharmacists play a critical role in improving biosimilar access, while contributions from pharmacists working in other settings is negligible.
   a. True
   b. False

4. How can a pharmacist in an interprofessional team facilitate biosimilar use?
   a. Serve as medication experts.
   b. Educate other healthcare professionals on the benefits of biosimilar adoption.
   c. Support the adoption of biosimilars directly via participating in P&T committee with other HCPs.
   d. All of the above

5. **True or False**: Biological agents for rheumatoid arthritis are often first-line treatments and do not require any additional prior authorization for patients.
   a. True
   b. False

6. **True or False**: Like the generic-brand relationship, biosimilars have identical chemical structures to reference products.
   a. True
   b. False

7. Which of the following is a challenge to the uptake of biosimilars?
   a. Nocebo effect
   b. Medication naming and labeling confusion
   c. Payor reimbursement
   d. All of the above

8. Which of the following is a reason pharmacists should care about increasing the use of biosimilar uptake regardless of practice site?
   a. They could help improve prescribers' and patients' confidence in biosimilar use.
   b. Pharmacists are not medication experts; moreover, it's not in the job description.
   c. They make money from using the more expensive reference biologicals, so it's a conflict of interest.
   d. The use of biological products has been and is continuing to decline.

9. **True or False:** A major barrier to biosimilars' use is higher immunogenicity rates compared to their reference biologic medications.
   a. True
   b. False

10. Did the activity meet the stated learning objectives? (if you answer no, please email sarahs@pswi.org to explain)
    a. Yes
    b. No

11. On a scale of 1 – 10 (1-no impact; 10-strong impact), please rate how this program will impact the medication therapy management outcomes or safety of your patients.

12. On a scale of 1 – 10 (1-did not enhance; 10-greatly enhanced), please rate how this program enhanced your competence in the clinical areas covered.

13. On a scale of 1 – 10 (1-did not help; 10-great help), please rate how this program helped to build your management and leadership skills.

14. How useful was the educational material?
    a. Very useful
    b. Somewhat useful
    c. Not useful

15. How effective were the learning methods used for this activity?
    a. Very effective
    b. Somewhat effective
    c. Not effective

16. Learning assessment questions were appropriate.
    a. Yes
    b. No

17. Were the authors free from bias?
    a. Yes
    b. No

18. If you answered "no" to question 17, please comment (email info@pswi.org).

19. Please indicate the amount of time it took you to read the article and complete the assessment questions.

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