



Biosimilar medicines uptake: The role of the clinical pharmacist

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ABSTRACT

The introduction of biological medicines has revolutionized the management of chronic diseases. Due to the high cost of biological medicine coupled with the fact that patents of many of these medicines are on the verge of expiration, manufacturers are exploring the production of biosimilars. The introduction of biosimilars has the capacity to increase competition among manufacturers, reduce prices, and improve patient access to these medicines. Therefore, a biosimilar is a new wave in therapy and treatment for the next few years. Despite the growing number of biosimilars approved for patient care, physicians' comfort in prescribing reference products against biosimilars and patient reluctance to switch from a reference product to a biosimilar are the major barriers for biosimilar increasing use. This paper aims to highlight the role of the clinical pharmacist (CP) in the utilization of biosimilars and the need for a pharmacy specialty regarding biosimilars. Of all the healthcare providers, CP has the most holistic view of the biosimilar products' clinical profile, and logistical and supply chain considerations. Thus, CPs are uniquely positioned to better educate all biosimilar medicine key stakeholders in an effort to increase access and rational use.

1. Background

The introduction of biological medicines has revolutionized the management of chronic diseases worldwide. These products are widely used to treat a variety of long-term medical conditions, including cancer,^{1–3} anemia of chronic renal failure,³ endocrine disorders,³ uveitis,³ ankylosing spondylitis,^{3,4} inflammatory bowel disease,^{3–7} psoriasis,^{3,4,8} rheumatoid arthritis,^{3,4,9,10} among others.³ The high cost of these biological medicines and the recent expiration of patents of many of them has spurred manufacturers to explore the production of biosimilars. However, the introduction of biosimilars has the capacity to escalate competition among manufacturers, reduce cost, and improve patient access to medicines.¹¹ Thus, biosimilars could represent the new wave in the management of long-term diseases for the next few decades.

A biosimilar is a biological medicine that contains a version of the active ingredient of an already approved original biotherapeutic medicine (otherwise known as the innovator or reference product).¹² In other words, a biosimilar is a biological product that is similar to the innovator version and has no clinically significant differences as demonstrated by structural and clinical trial comparisons of the products. A biosimilar is similar to its reference product in purity, chemical and biological activities, and potency. Acceptable minor variations in clinically inert ingredients can exist between the innovator and the biosimilar products. These minor differences are an inevitable event during the production process for both innovator and biosimilar products. In addition, developing identical copies of

biological molecules is impossible due to their heterogeneous and complex nature, high molecular weight, and batch-to-batch variations. Thus, biosimilars are not generics of the original biological medicines. Although just as generics of small-molecule medicines have helped to cushion cost and increased patient access to treatment, opportunities exist for biosimilars to improve healthcare worldwide.

2. The role of clinical pharmacists and their impact on generics utilization

The emergence of generic medicine created an opportunity to reduce the cost of medications. In spite of this, there was palpable fear about the quality, safety, and efficacy of generic medicines, and misconceptions that stemmed from a lack of understanding on how generics differed from brand name products by both physicians and patients/consumers.¹³ Hence, the need for aggressive clinical pharmacists' educational interventions to help address these concerns and promote generics utilization. Good pharmacist-physician-patient relationships have helped to clarify that generics are identical to brand name medications with regard to quality, safety, and efficacy. This has in turn led to increased familiarity with and knowledge of generic medications thereby making them more acceptable by physicians and patients. Clinical pharmacists (CPs) have played a crucial role in increasing generic utilization by providing information about the potential cost savings associated with generics to patients as well as health insurance companies, and increased generic substitutions and dispensing.¹⁴ However, it is noteworthy that in 2002, CPs' face-to-face discussion on availability, clinical benefits, and cost-saving of generics with 1770 physicians from 10 states in the U.S. encouraged their use as

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first-line treatment.¹⁵ Another study conducted in the U.S. showed that CPs' patient educational intervention to increase awareness on the low cost of the generic alternative resulted in increased uptake of lower-cost generic antihypertensive medications in the intervention group.¹⁶ In the UK, pharmaceutical counseling provided to 39 physicians led to the generic prescription median change of 5.37% among the physicians in the intervention group as against 1.61% in the control group.¹⁷ Additionally, evidence from the literature demonstrated that CPs' educational and communication interventions significantly decreased the rate of brand switch-backs.¹³

3. Emergence of biosimilars

Interestingly, the gap created by the expirations of patents of a significant number of reference biological medicines recently has ignited the heightened interest of manufacturers in biosimilars. Literature review revealed that as of June 2020, 58 biosimilar medicines have been approved in the European Union (EU),¹⁸ while 29 biosimilar medicines received approval in the U.S.¹⁹ In Canada, 25 biosimilars of 12 reference products were approved as of August 2020,²⁰ whereas Australia ranked highest with 27 biosimilars receiving approval in the year 2020 alone.²¹ Although biosimilars have the capacity to reduce healthcare costs in chronic disease management, they face uptake challenges. Despite the growing number of biosimilars approved for patient care, physicians' comfort in prescribing reference products against biosimilars, biosimilar interchangeability, patient caution, and hesitation to switch from a reference product to a biosimilar, and payer considerations are major factors responsible for biosimilar current low utilization.^{4,22–24} Consequently, several countries have implemented policies, especially education initiatives to enhance their use.²⁵

Clinical pharmacists (CPs) are uniquely positioned to play a key role in educating relevant stakeholders towards overcoming the barriers and enhance uptake of these novel agents. A clinical pharmacist is a good communicator and a medication expert who knows the most appropriate source of information about the use, therapeutic and adverse effects, mode of action (MOA) and administration, storage and dispensing, regulation of all medicines, including biologics and biosimilars.²⁶ Given the complexity of biosimilar medicines, ensuring their safety and efficacy is critical. It is important for pharmacists, especially CPs to remember that efficient actions on their part will mean excellent outcomes for the adoption of biosimilars.

Better adoption of biosimilars in clinical practice will occur as clinicians, patients and other key stakeholders increase their understanding of the role of biosimilars in patient care. Though the path to biosimilar uptake may not be straight, pharmacists, especially CPs are positioned to take a lead. This paper aims to highlight the role of the CPs in the utilization of biosimilars and the need for a pharmacy specialty regarding biosimilars.

4. The roles of clinical pharmacists in the utilization of biosimilar medicines

Just like generics, the slow uptake may be due to physicians' and patients/consumers' concerns about the equivalence of quality, efficacy, and safety of biosimilars to the originator brand. Against this backdrop, clinical pharmacist as a medicine expert has a vital role to play in order to enhance the utilization of biosimilars:

4.1. Making formulary decisions about biosimilars

Addition of biosimilars to the health system formulary is an integral process that has to be perfected to successfully introduce biosimilar into patient care. Obviously, this cannot be achieved without a CP as an integral member of the pharmacy and therapeutic committee (PTC) in the hospital settings. The formulary evaluation process may be used to add a biosimilar to the formulary as an alternative to or a replacement for an innovator medicine.

It is noteworthy that CPs do not focus only on the pharmacotherapy of biosimilars, but assess all aspects of pharmaceutical care when deciding to add biosimilars to the hospital formularies. Therefore, CPs are well placed to take a leadership role in an interprofessional effort to evaluate

biosimilars for use in healthcare facilities through the formulary process for increased access to patients. Because biosimilars are not completely identical to the innovative product, an objective analysis of comparative data demonstrating the efficacy and safety (especially immunogenicity) of a biosimilar for specific patient populations treated at the institution is needed to be conducted by the PTC with a CP taking a lead.

4.2. Assessment of the credibility and reliability of suppliers

Of all the healthcare providers, CP has the most holistic view of the biosimilar products' clinical profile and logistical and supply chain considerations, for example, shelf life, storage among others. Thus, for the successful implementation of biosimilars in clinical practice, CPs can play an important role in assessing the credibility and reliability of suppliers to ensure the safety and efficacy of biosimilars supplied to healthcare institutions.

4.3. Biosimilar medicine literature search and evaluation

The CPs have the capacity to provide valuable input into decisions about the proper use of biosimilars in the healthcare facilities based on available comparative quality, preclinical, and clinical studies data. Clinical pharmacists can evaluate biosimilar clinical data and apply them to raise issues that physicians might not contemplate at all. To stay abreast, CPs can search and review the most recent biosimilar approval resources to be able to timely recommend biosimilars of proven indications or alert physicians when no good literature exists to support their use.

4.4. Clinical trials of biosimilars

The CP can play a huge role as a member of a multidisciplinary team in conducting clinical trials to demonstrate that biosimilars have the same MOA, pharmacokinetics, and pharmacodynamics characteristics in the clinically tested and extrapolated indications in addition to addressing any expected differences in toxicity or effectiveness.²⁷

4.5. Storage and dispensing of biosimilars

Clinical pharmacists are specifically responsible for the safe storage and appropriate dispensing of medicine, including biosimilars in healthcare facilities. Biologicals are stored under low temperature and CPs can ensure that good storage and distribution practices are strictly observed to guarantee their safety and efficacy. For example, it is recommended that Adalimumab and its approved biosimilars should be stored at 2–8 °C for two years.^{28–32} Although in a peculiar situation where there is no facility for refrigeration, these products may be stored at room temperature (25 °C) with protection from light for 14 days or less.^{28–32}

4.6. Provision of education to key stakeholders about biosimilars

Dissemination of drug information to key stakeholders (physicians, nurses, other pharmacists, pharmacy technicians, patients, payers, and policymakers) for clinical use of medicines including biosimilars is the sole responsibility of the CPs.³³ As biosimilars differ from generic medicines, it is imperative that healthcare professionals involved in their use have adequate critical information about their prescribing practices, traceability, and interchangeability. The information provided must be tailored according to the characteristics of each stakeholder for meaningful education to occur:

4.6.1. Physicians

To ensure that the patients are being prescribed the safest and most efficacious treatment possible, the physicians (prescribers) will need to understand the complexities of biosimilars and take decisions that will be in the patient's interests. Acceptance and use of biosimilars hinge on the comfort level of the physicians after evaluating comparative data.³⁴ Nevertheless; physicians may require additional information from CPs to make a decision about biosimilar use.

Moreover, CPs are better placed to provide information to physicians on what is available and the interchangeability of reference products and biosimilars in accordance with each country's policy on interchangeability. Overall, education from a CP can lead to higher levels of trust, confidence, and increasing physicians' acceptance of biosimilars and ultimately rational prescribing.

4.6.2. Nurses

Nurses as one of the frontline healthcare providers are challenged every time a novel medicine, such as biosimilars are introduced into clinical practice.³⁵ Nurses will have the opportunity to play key roles in this new era of biosimilars in the area of administration and education. Thus, due to the complex nature of biosimilar medicines, education regarding these products needs to be provided to nurses by CPs for effective pharmaceutical management in the hospital settings.

Clinical pharmacists drawing from their medication expertise can educate nurses to understand what biosimilar medicines are, their efficacy, and safety profiles to empower them to accurately reinforce patient education. This is so because an informed nurse can help alleviate patients' concerns and optimize the expected benefits of biosimilars for patients in particular and healthcare systems at large. Also, an informed nurse can effectively interface between the physician and patient, especially when biosimilar treatment regimens are initiated or modified to ensure positive patient health outcomes.

4.6.3. Other pharmacists

The advent of biosimilar medicines presents a unique and unprecedented opportunity for the pharmacy profession to improve patient care. Thus, non-clinically-oriented pharmacists working in all settings will need to be educated about biosimilar medicines by CPs to help escalate their use and prevent inappropriate utilization.

4.6.4. Pharmacy technicians

Pharmacy technicians also should be educated by CPs to help reduce the risk for look-alike and sound-alike errors in dispensing biosimilars.

4.6.5. Patients

When patients are prescribed biosimilars, they are unaware of the implications of this treatment. Often, patients are not provided with a complete explanation of the choice of therapy selected for their conditions and treatments. Patients' education and counseling are among the main responsibilities of the CPs. Most patients have a reasonable understanding of the concept of generic medications. Conversely, substantial education from a CP will be required to assist patients in understanding the differences between generics and biosimilars.³⁶ Adequate patient education and counseling when initiating therapy or switching to a biosimilar are critical. Without appropriate pharmaceutical care (patient-centered education and guidance), most patients may have a perception that a biosimilar is less effective than the innovator product. Clinical pharmacists have the potential to change patients' beliefs (e.g. that switching to a biosimilar and indication extrapolation, respectively are safe and effective) and behaviors (e.g. positive framing of biosimilar conversations with patients). The uptake of biosimilars by patients can be significantly improved with the involvement of a CP who can help educate and guide the patients, as well as help, ensure the patient adheres to the biosimilar therapy and the care plan. Clinical pharmacists can also help patients understand the complexities of these biological therapies and also help them navigate the payment process. Without doubts, patient interest in biosimilars probably will be positively influenced by education from a CP.

4.6.6. Payers

Payers are likely to feel economic pressure to use biosimilars, but CPs can assure them of their clinical efficacy and safety. Also, acceptance and use of biosimilars depend on the comfort level of payers after evaluating comparative data.³⁴ Clinical pharmacists can engage with health insurance companies for adequate biosimilar coverage to ensure better care for

patients. Ensuring that patient receives appropriate biosimilar that aligns with their health insurance company's formulary will be paramount to guaranteeing access and affordability.

4.6.7. Policymakers

Clinical pharmacists can help educate policymakers to make regulations and laws that will help improve the uptake of biosimilars. Awareness of the scientific and quality considerations associated with biosimilars can help policymakers weigh various stakeholders' competing interests, including the need for new product development, interchangeability, affordability, access to medicines, and protection of public safety.³⁶

4.7. Biotherapeutic monitoring and pharmacovigilance

Clinical pharmacists are directly involved in biotherapeutic monitoring, evaluating patients for efficacy or signs of immunogenicity or toxicity. Post-marketing pharmacovigilance is needed for biosimilars because of the potential for a unique adverse effect profile that differs from that of the innovator product. Rare but potentially serious adverse events are unlikely to be detected before the marketing of biosimilar medicines.³⁷ Clinical pharmacists are in a pivotal position to enable the collection of pharmacovigilance data and post-marketing monitoring in many countries.^{33,38-40} Clinical pharmacists can provide feedback to the regulatory bodies on biosimilar safety through adverse event reporting and other discussion fora. Furthermore, CPs can submit case studies on interchangeability and pharmacovigilance, which can inform guidance documents.

4.8. Biosimilar documentation

Documentation is a critical component of pharmaceutical care. Therefore, adequate involvement of CPs in biosimilar use is important to ensure that all identification information such as the name of the product, batch number, the manufacturing company, indication among others about the dispensed biosimilar are retained in the pharmacy. The CP is the more appropriate healthcare provider to document the unique proprietary name, manufacturer name, lot number, and country of origin of biosimilars as recommended by WHO for traceability.⁴¹ Lastly, presenting signs of biosimilar adverse reactions can also be documented by a CP for follow-up studies on the post-approval products.

5. The need for a specialty pharmacy regarding biotherapeutics

The introduction of multiple biosimilars in patient care has challenged all healthcare providers, especially the CP to stay informed to be able to inform others. Therefore, CP must have a fundamental understanding of biosimilar medicines to be in a position to implement them and educate other pharmacists, other healthcare providers, and patients about their use. Because of nature of biosimilars that often require specific handling and storage techniques and the significant role of the CPs in increasing their adoption for patient care, there is an urgent need for the creation of biotherapeutic pharmacy specialty worldwide for effective and efficient biological pharmaceutical care. Additionally, development of curriculum for this specialization which includes topics such as Biomolecules and Cell Structure, Molecular Genetics, Cell and Tissue Culture, Gene Technology in the Pharmaceutical Sciences, and Regulatory Affairs among other important topics is recommended.

6. Conclusion

Understanding of the nature of reference biologics and how they relate to their biosimilar counterparts is still challenging for all the key stakeholders. Though the path to biosimilar uptake could be tortuous, CPs are positioned to take a lead. Clinical pharmacists can play an important role in educating key stakeholders to ensure the safe, effective, and cost-effective use of biosimilars in clinical practice. As medicine specialists, CPs are expected to lead discussions with physicians and patients on the

interchangeability of innovator biologics with biosimilars. Above all, CP will be a resource to answer questions regarding the appropriate use of biosimilars, and it is important that individual CP is knowledgeable enough to provide sufficient recommendations. Thus, the need for a pharmacy specialty dedicated to biotherapeutics.

Declaration of Competing Interest

The authors do not have any conflicts of interest or financial interests to disclose.

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