

What to do about BIOSIMILARS?

Plan sponsors have new options for cost savings, but switching from reference biologics remains a significant concern

By Suzanne Lepage

With a number of biologic drugs facing patent expiration, plan sponsors will have a lot to think about when it comes to considering how to deal with biosimilars. What are some of the considerations for their drug plans as they look at the issue in 2017?

Regulatory issues

As participants at *Benefits Canada's* recent Face to Face Drug Plan Management conference demonstrated, the industry is well aware of the fact that biosimilars aren't the same as generic drugs. During a live-polling session on myths in drug plan management at the conference, 97 per cent of participants disagreed that biosimilar and generic drugs are the same thing.

That's good because Health Canada, which determines which drugs are interchangeable, doesn't deem biosimilars to be bioequivalent to, and it doesn't recommend substituting them for, the brand-name biologic. Its position is only a recommendation because the regulations that allow pharmacists to substitute drugs rests with provincial authorities.

Because Health Canada declares generic drugs to be bioequivalent to their brand counterparts, provincial regulations allow pharmacists to switch to them. While no province has implemented guidelines or regulations regarding biosimilar substitution, that may change as governments explore alternatives and develop policies to save on biologic drug costs.

Pricing

The pan-Canadian Pharmaceutical Alliance's primary function is to conduct confidential negotiations

with pharmaceutical manufacturers to generate savings via product listing agreements for publicly funded drug programs. But when it comes to agreements for biosimilars, the alliance has mandated manufacturers to reduce the drug's price for all payers, including private drug plans. The manufacturer of a reference brand-name biologic has the opportunity to offer similar transparent price reductions to gain an equivalent listing status. Negotiations have yet to conclude for the three most recent biosimilar drugs approved by Health Canada.

Design considerations for new patients

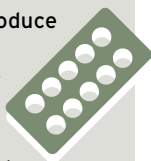
Drug plan design can encourage plan members who are starting on a biologic to take a biosimilar. The options include:

- 1)** Step therapy, which requires plan members to try less expensive medications, such as the biosimilar, first. If they can't tolerate or fail on the biosimilar, their plan will then allow access to the brand-name biologic.
- 2)** Preferential listing of biosimilars requires new patients to use them instead of the brand reference biologic. The approach can limit choice and access to brand-name biologics if the price is similar, however.
- 3)** Some plans will limit reimbursement for the brand-name biologic to the price of the biosimilar. Commonly known as reference-based pricing or maximum allowable cost, the approach provides that if plan members prefer the brand-name biologic, they must pay the difference.
- 4)** A listing agreement with the brand-name biologic manufacturer can ensure the price of the reference drug is on par with the biosimilar and allows the choice of either product.



BIOSIMILAR BASICS

- To make a biologic drug, manufacturers use living cells that are programmed to create the product, rather than the chemical-mixing process used to produce traditional medications. They're larger molecules that are much more complex and very sensitive to minor changes in the manufacturing process. Very small changes have the potential to affect the safety of a product and the way it will function in a patient's body.
- In the past, Health Canada used the term subsequent-entry biologics. It recently aligned with the rest of the world to use the term biosimilar.
- According to Health Canada, a biosimilar is a "biologic drug that enters the market after a previously authorized brand version in Canada, and with demonstrated similarity to that reference biologic drug." Because it's difficult to replicate the manufacturing process for biologics, the products will be similar but not the same.



patient developing anti-drug antibodies, which could limit treatment effectiveness and compromise patient safety."

There have been studies on switching, including one conducted by researchers at Western University in London, Ont., that dealt with Remicade. According to Dr. Brian Feagan, a gastroenterologist at London Health Sciences Centre and a professor of medicine at Western, the study adds to the body of knowledge about switching between reference biologics and biosimilars but he notes there are limitations to the results. "The study pooled the results for six [of the eight] approved indications together and did not differentiate the impact of switching on these very different diseases," he says.

"When the endpoints are pooled together, this study is not statistically powered to detect the disease-worsening differences between conditions, and the generalized result may not be a true measure for each one. The study also considered only a one-way switch from a reference biologic to its biosimilar and does not inform on the impact of switching back and forth between the brand and the biosimilar or between different biosimilars."

The study only provided data on the impact of switching in regards to six of the conditions that Remicade treats. It doesn't extrapolate to apply to other conditions where biosimilars exist, such as oncology and diabetes.

Canadian action on biosimilars

In Canada, the uptake for biosimilars has been minimal, despite the fact that Health Canada has approved five of them. That's not surprising to Michael Brogan, president of QuintilesIMS Canada. "Inflectra, the first significant Canadian biosimilar, was approved in 2014 and only received its first public listings in February 2016," he says.

In Canada, initial approval for Inflectra didn't include gastrointestinal indications. "We see effectively zero penetration of the gastrointestinal market, and although Health Canada granted the new indications in June 2016, the review and negotiation process is not complete and, as a result, we do not yet see uptake in the new indications," says Brogan.

According to Brogan, many payers' policies require or encourage new patients to use the biosimilar over the biologic but they generally don't ask those currently taking the reference drug to switch. Since a small percentage of patients will be new, the uptake of biosimilars will lag, he notes.

For plan sponsors considering the issue, it's important to note that not every biosimilar will be the same and the dynamics of the therapies will affect the uptake. A biosimilar medication to treat a chronic disease, for example, will generate limited switching and uptake, whereas a treatment for an acute condition regularly prescribed to new patients can have a bigger impact.

With a large number of biosimilars in the pipeline, the landscape for drug plans is shifting. However, unless the uptake for biosimilars in Canada increases, the market may continue to lag, according to Jim Keon, president of Biosimilars Canada. "Unless payers develop coverage policies that encourage biosimilar use, such as preferentially listing biosimilars as first-line treatment, biosimilar manufacturers may not see Canada as a promising market and choose not to bring their products here," he says.

Stephen Frank, senior vice-president of policy at the Canadian Life and Health Insurance Association, expresses a similar

For plan sponsors, while they may often look to their insurance carrier or pharmacy benefit manager to recommend plan design options to deal with biosimilars, Alan Kyte, a senior pharmacy consultant at Willis Towers Watson, suggests they should still "inform themselves of the policies, as there are several different approaches, each with its own merits and challenges."

Concerns for existing patients

Plan sponsors could generate additional savings if plan members who currently take biologics switched to biosimilars. There are significant concerns about switching, however.

"According to the product monographs, there may be significant differences between the brand biologic and the biosimilar, including dosing, packaging and side-effect profiles," says Bev Herczegh, a pharmacist and director at the Pangaea Group who frequently conducts continuing education programs on biosimilars.

"It will be important for physicians and pharmacists to understand the impact of these differences when switching patients between products to ensure patient safety and outcomes."

A normal immune response makes antibodies to clear infections, but because biologic drugs are primarily protein products, the body may identify them as foreign substances and fight against them, provoke an allergic response or experience adverse side-effects. The immune system could also destroy the proteins, potentially rendering them ineffective.

"We don't know if switches between biosimilars and originator product may increase immunogenicity," says rheumatologist Dr. Jane Purvis, referring to the ability of a substance to provoke an immune response.

"Slight differences between the products could result in the

HOW ARE OTHER JURISDICTIONS DEALING WITH BIOSIMILARS?



U.S. interchangeability guidelines delayed

In the United States, the Food and Drug Administration has already approved four biosimilars but it continues to delay its promised draft guidance on the issue of interchangeability. Because individual states regulate pharmacist substitutions and switching, the delay has resulted in 24 jurisdictions, including Puerto Rico, enacting laws that permit some form of substitution to encourage the use of biosimilars.



Tendering process in Norway

According to a 2015 National Prescription Drug Utilization Information System market intelligence report on biologic response modifier agents, the uptake for biosimilars has been higher in many Organisation for Economic Co-operation and Development countries than in Canada.

Usage in Norway is particularly high. That country has a centralized single-payer system that allows the government to manage its drug plan through a tendering process. As a result, it can negotiate to cover only one preferred product and achieve substantial savings by essentially requiring patients to switch in order to receive reimbursement for their treatment.

According to Jim Keon, president of Biosimilars Canada, that type of low-cost tendering process wouldn't be sustainable in larger countries.

"There is such a high cost to bring a biosimilar to market, manufacturers would not be able to sustain the lower prices needed to win the tenders," he says.

concern. "Without biosimilar competition, brand-name biologic prices won't be driven down when their patent expires," he says.

"We need to find ways to encourage a strong biosimilar market in Canada."

But Geoff Sprang, executive director for value, access and policy at Amgen Canada Inc., emphasizes the need to allow for patient choice. "As a manufacturer of both branded and biosimilar medications, we believe that benefit plan designs should offer physician and patient choice to pick the most appropriate treatment," he says. "For example, if there is a difference in cost between the biologic and the biosimilars, patients should have the choice of paying the difference to receive the biologic drug if they choose. The field of upcoming biosimilar competitors is extremely deep, and allowing originator brands to compete will only benefit plan sponsors and employees. Simply put, if a biosimilar manufacturer doesn't have to compete for business, consumers aren't going to get the best deal."

Suzanne LePage is a private health plan strategist who regularly writes and speaks about issues related to drug plan management.

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Foyston, Gordon & Payne Inc.
1200 McGill College Ave, Suite 1100
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