



INSIDE STORY[®]

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The drug landscape is changing... Say hello to subsequent entry biologics

Amazing. This is certainly an accurate depiction of biologics. On the one hand, biologics are amazing because they represent a new class of drugs that has the potential to improve the lives of patients suffering from a number of serious conditions. However, on the other hand, most biologics are also amazingly costly.

Fortunately, the drug landscape just got brighter as a small number of subsequent entry biologics (SEBs) have entered the Canadian market with numerous more on the horizon. Also known as “biosimilars” and “follow-on biologics,” SEBs have the potential to deliver the same amazing health outcomes as biologics, but at significantly lower costs.

Although SEBs represent a good news story, even positive change can seem daunting so here’s an overview of today’s drug landscape in relation to SEBs...

Pharmaceutical industry trends

The development of drugs for treating rare diseases has been rising steadily. Increasingly these breakthroughs are possible due to the development of the class of drugs called biologics. And now we’re also seeing biologics for more common health conditions like high cholesterol and asthma. For instance, new PCSK9 inhibitor drugs can lower cholesterol by as much as 70%.¹ And there are numerous other impactful biologics in the pipeline.

However, as we also know, the unique nature and high effectiveness of biologics comes at a cost—a very high cost. This presents a particularly challenging situation for plan sponsors as they strive to provide plan members with the best treatment options that advances in medicine can provide, while at the same time effectively managing plan costs now—and into a much more expensive future.

Costs

Although over the next decade, biologics are expected to represent upward of 20%² of the pharmaceutical market, which in turn will put financial pressure on plans, relief is on the horizon in the form of SEBs. As we see various biologics come off patent, we will also see more SEBs entering the market. In Canada, by 2020, numerous patents³ will expire and several global pharmaceutical manufacturers are in the process of developing, or see this as an opportunity to develop, further SEBs.

So what does this really mean in terms of cost containment? The complexity of

SEB Savings

Originator Biologic	SEB	Price Difference
Lantus	Basaglar	15%
Neupogen	Grastofil	17%
Enbrel	Brenzys	25%
Remicade	Inflectra	47%

developing, manufacturing, and testing biologics, as well as intensive regulatory requirements mean that the percentage price difference between an SEB and its biologic originator will not be as substantial as the price difference between a generic and its brand-name counterpart. However, experts still predict significant savings based on the experience in some European countries where SEBs can cost significantly less than originator products. So far, in the Canadian market SEBs are resulting in major savings. For example, the SEB Inflectra costs 47%⁴ less than its originator biologic Remicade. And a recent addition to the Canadian market, the SEB Brenzys costs 25%⁵ less than its originator biologic, Enbrel. The average annual cost for originator biologics ranges from about \$1,500 for Lantus to as much as \$20,000 to \$30,000 for drugs like Enbrel and Remicade. Given that the annual cost of biologics across an employee group could run into the hundreds of thousands of dollars, the savings realized by SEBs are absolutely vital to health benefits plans.⁶

More SEBs in the Canadian market means equally effective drug treatment options for your plan members and lower costs for your plan—so far, so good.

SEBs on the Horizon... Arriving by 2020⁷

Drug	Brand Name (Originator Drug)	Indication(s)
Adalimumab	Humira	<ul style="list-style-type: none"> → Crohn's disease → Rheumatoid arthritis → Psoriatic arthritis → Ankylosing spondylitis → Chronic plaque psoriasis → Polyarticular juvenile idiopathic arthritis
Bevacizumab	Avastin	<ul style="list-style-type: none"> → Metastatic colorectal cancer → Metastatic or recurrent non-small cell lung cancer → Glioblastoma → Epithelial, ovarian, fallopian tube, or primary peritoneal cancer
Cetuximab	Erbix	<ul style="list-style-type: none"> → Head and neck cancer → Metastatic colorectal cancer
Epoetin alfa	Eprex	<ul style="list-style-type: none"> → Anemia
Pegfilgrastim	Neulasta	<ul style="list-style-type: none"> → Neutropenia
Ranibizumab	Lucentis	<ul style="list-style-type: none"> → Age-related macular degeneration → Diabetic macular edema → Macular edema secondary to retinal vein occlusion
Rituximab	Rituxan	<ul style="list-style-type: none"> → Non-Hodgkin lymphoma → Chronic lymphocytic leukemia → Rheumatoid arthritis → Granulomatosis with polyangiitis
Trastuzumab	Herceptin	<ul style="list-style-type: none"> → Breast cancer → Metastatic gastric cancer

Safety

European Union (EU) adoption of SEBs is much further along than in North America; however, the rate and degree of that adoption varies across EU countries. Experts think that this is due to a number of variables, such as differences in local reimbursement policies and pricing. In addition, physicians may be reluctant to prescribe SEBs due to lack of awareness and education regarding SEBs overall—and in particular regarding SEBs' safety in relation to their originator biologics. Although SEBs are approved to the same standards as their originator biologics, worries persist among some.

This points to the need for more education. Fortunately, these days it's a small world, so physician education is occurring across borders. Physicians in North America are gaining insight into SEBs through the European experience. As a result, North American physicians may be more familiar with SEBs than European physicians were before SEBs were launched in Europe.

In addition, as always, physician education and awareness will rely heavily on the scientific evidence. The evidence is clear that an SEB is not identical to its originator biologic; it is not a "generic biologic." Manufacturers of the innovator drug are not required to share their original formula, so it is difficult to produce an identical replica of the innovator drug.

However, in fact, even the formulation of the originator biologic changes multiple times over its lifespan essentially creating a slightly different drug each time. Known as "product drift," this happens as a new batch of a biologic is formulated and adjustments are made to its manufacturing. These adjustments are made within certain limits and are not significant enough to warrant re-testing of the biologic. Therefore, an originator biologic product manufactured today will naturally differ from the same originator product produced by the same manufacturer several years ago.

It is accepted that when it comes to biologic and SEB drugs, variation is simply part and parcel of the production process, but that ultimately the therapeutic effect must remain constant. As a result, similar to a SEB being "close but not identical to" the originator biologic, likewise an originator biologic and new batches of that same biologic may become less—or more—similar over time.

Accordingly, physician prescribing will also look to regulators for direction. For example, Health Canada's current position: "Health Canada does not support automatic substitution of a Subsequent Entry Biologic for its reference biologic drug and recommends that physicians make only well-informed decisions regarding therapeutic interchange."⁸

In addition to alleviating safety concerns, another impetus for physician prescribing will be reimbursement policies that encourage the use of SEBs.

NOR-SWITCH Study⁹

The Norwegian government funded a study called the NOR-SWITCH trial to examine the efficacy and safety of switching from the originator biologic infliximab to the SEB. Between October 6, 2014, and July 8, 2016, researchers followed 481 patients who, via random assignment, took either the biologic or SEB. The preliminary data recently presented by researchers showed that the SEB was not inferior to continued treatment with the biologic.

DANBIO Study¹⁰

The DANBIO registry is a nationwide registry in Denmark that includes more than 95% of all patients with inflammatory arthritis under medical care. In 2015, to save costs, the Danish government decided to switch all patients treated with the originator biologic infliximab to the SEB. For three months before the switch—as well as the switch and for three months after the switch—researchers examined disease activity measures in 647 patients. Findings include that although there were trends towards changes in the disease activity measures, they were not clinically relevant. The study is still ongoing.

Rigorous Review Process

Before an SEB can become a preferred product on GSC plans, it must undergo GSC's extensive review process and be deemed high quality with strong evidence around safety and efficacy. Individual review and critique on a product-by-product basis drives our decision making.

Case in point: Inflectra as a preferred product

As covered in an April 2016 GSC Update, after considering the evidence, as well as the implications and alternatives for covering SEBs, we developed our approach:

- SEBs are listed as preferred products under our formularies. The originator biologic will be covered only in exceptional circumstances.
- This policy applies to new starts on the medications; patients on the originator biologic will be grandfathered.
- Inflectra is listed, and the policy will apply later this year for Brenzys (for the originator Enbrel) as well as other SEBs like Basaglar (for the originator biologic Lantus) and Grastofil (for originator Neupogen).

As more SEBs come off patent, we expect to list more of them to drive down plan sponsor costs while ensuring plan members receive the most appropriate biologic for their conditions.

Reimbursement policies

In the public and private payor world, reluctance to assign preferred status to SEBs in plan designs (reimbursing to the price of the SEB, not the originator product) represents a barrier to SEB prescribing, and in turn, a deterrent to establishing a viable market for SEBs in Canada—one that is desperately needed. As long as coverage for the original biologic exists on drug plans, physicians are less likely in the near term to change their prescribing practices, thus impacting the viability of the SEB market and the potential savings that can be gained.

Both private and public payors are faced with the challenge of establishing appropriate SEB reimbursement policies. Taking a stand, the pan-Canadian Pharmaceutical Alliance (pCPA)—formerly known as the Pan-Canadian Pricing Alliance and the Generic Value Price Initiative and now collectively the pCPA—issued *Subsequent Entry Biologics (SEBs) First Principles* on April 1, 2016.

The principles state that: “Consistent with its mandate that includes increasing patient access to clinically and cost-effective drug treatment options, the pCPA will encourage a competitive environment that includes SEB market growth and is conducive to **long-term cost reductions** and sustainability for public drug plans.”¹¹ Acting as a central and dominant hub, the pCPA is providing a framework for adoption by the other provincial plans. An example is Inflectra, which was negotiated by the pCPA and is now available on various public plans across Canada at 47% of the price of Remicade.

So will private plans follow suit? Instead of supporting the adoption of SEBs, some carriers have engaged in deals—known as product listing agreements—with the originator biologic manufacturers as a way to offer originator biologics at a discount to plan sponsors.

GSC believes that these deals represent a case of short-term thinking. Although product listing agreements bring down the cost of a biologic today, so some gains—these gains have long-term consequences because a lack of preferential coverage for SEBs means that SEBs may not reach the adoption levels necessary to establish a viable SEB market in Canada. Of course, without a viable market, manufacturers may not see enough incentive to bring future SEBs to market in Canada.

In the big picture, this means fewer options for plan members to get the help they need as all available options are at a high cost—even with the biologic deal discounts. In addition, transparency surrounding product listing agreements continues to be troubling. It's not disclosed what the actual financial terms of the deal are and whether the full extent of the savings is passed on to plan sponsors and through what mechanisms. Specifically, how are the savings associated with product listing agreements incorporated into stop loss pricing? What mechanisms exist to ensure viability of future savings once the deal with the originator product expires? These are all questions for which the answers are not clear at the moment.

Preferential placement of SEBs on formularies provides a triple bonus: (1) it delivers maximum **transparent** savings directly to plan sponsors, (2) it provides plan members with additional treatment options, and (3) it helps grow and establish the market for SEBs in Canada.

GSC is one of the first major benefit carriers in Canada to list the SEB Inflectra as a preferred product for plan members newly prescribed the anti-inflammatory drug Remicade. Our very own GSC pharmacy strategy leader, Ned Pojskic, was recently quoted as he explained the GSC decision: "Our first principle is always plan member safety, and we are embracing SEBs as a whole as a valuable addition to the marketplace."¹² As always, we looked to the scientific evidence that clearly demonstrates the comparable safety and efficacy of Inflectra compared to Remicade.

It all comes down to change management

Will we see more access to SEBs or less? Although SEBs represent opportunity knock, knock, knocking, Canada is a relatively small market, so for SEB manufacturers to see the value of bringing these products to Canada, SEBs will need to be readily and steadily adopted. Ultimately, if we want more access to SEBs, we need to effectively manage change. Whether we realize these benefits will, to a large part, depend on our willingness to adopt reimbursement policies that promote their use. As they say, "If you change nothing, nothing will change."

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NO HARM SHOWN IN LIMITING BLOOD GLUCOSE TEST STRIPS

Given the high cost of blood glucose test strips, public and private payors have considered implementing quantity reimbursement limits on test strips, which are routinely used by diabetics to test blood sugar levels. However, the effects of reimbursement limits on patient outcomes has been unknown—until now. A recent study—*Association of a Blood Glucose Test Strip Quantity-Limit Policy With Patient Outcomes: A Population-Based Study*—found that the Ontario government’s quantity limit for blood glucose test strips is not associated with worsening short-term outcomes.

In 2013, when Ontario introduced quantity limits for blood glucose test strips, there were concerns that this could lead to poor diabetes management. However, the study found no increase in visits to emergency rooms in the short term by diabetics experiencing high or low blood sugar. These findings suggest that adopting limitations can help reduce costs associated with test strips without causing patient harm.

Although the study didn’t include private plans, the researcher recognizes that test strips are costly regardless of the type of payor and suggests that private plans could also save money by establishing limits. The researcher also advises that further research is necessary to ensure there are no adverse patient outcomes in the long term.

What does this mean for your plan? GSC already has a policy in place for the reimbursement of diabetic test strips. Introduced in December 2011, this policy limits the maximum number of test strips that GSC reimburses annually. The maximum depends on whether the plan member is insulin dependent or not. Plan members who require more than the annual maximum must have their doctor provide documentation supporting the medical need to GSC for assessment by our special authorization team.

For more information about the GSC diabetic test strips policy, contact your account team. For more information about the study, visit *JAMA Internal Medicine* at <http://jamanetwork.com/journals/jamainternalmedicine/article-abstract/2580721>.

NEW SLEEP SURVEY INVESTIGATES EMPLOYEE FATIGUE

Based on a Conference Board of Canada survey of 739 full-time and part-time employed Canadians, a new report called *Running on Empty: Understanding Fatigue in the Workplace*, reveals that lack of sleep and poor-quality sleep can affect individual health and wellbeing, as well as workplace safety, performance, and productivity. For instance, in terms of physical health, the report references research that links shorter sleep duration to obesity, diabetes, hypertension, cardiovascular disease, reproductive health, and cancer. The report also discusses research that links poor sleep with mental health conditions like depression and anxiety.

In terms of assessing how tired employees are at work and how fatigue may impact productivity, highlights include that 27% of survey respondents reported feeling tired most days or every day during a typical workweek. When asked about their productivity at work on days they were tired, 42% reported that their productivity and performance were

somewhat or significantly worse when they did not get enough rest. Respondents identified stress and job demands as the main cause of fatigue. Other leading factors included stress from demands at home, physical health problems, and poor sleep habits like caffeine before bed. In addition, compared to employees who did not have children living at home, employees with children under the age of 18 were more likely to report being tired or not having enough rest, and 15% of women indicated that they never went to work feeling tired compared with 29% of men.

Lessons learned from the report include that employers that proactively address their employees' fatigue will have a healthier, more productive workforce and a safer working environment. To do so, employers need to look at both work and non-work factors to gain insight into the issues contributing to employee fatigue and, in turn, to determine the best ways to prevent and manage it.

For more information, visit the Conference Board of Canada at http://www.conferenceboard.ca/press/newsrelease/16-09-20/almost_30_per_cent_of_canadians_go_to_work_feeling_tired.aspx.

STUDIES HIGHLIGHT THE NEED FOR DISEASE MANAGEMENT SUPPORT

Asthma Control in Canada, Survey, 2016

Although there is no cure, people living with asthma can lead normal and active lives as long as they manage the condition. However, a national survey commissioned by the Canadian Lung Association found that nine in 10 Canadians with asthma do not have it under control. Survey findings include that although Canadians with asthma agree that controlling asthma is their own responsibility, 41% do not exercise at all due to their asthma and 14% are not taking their medication as prescribed. Overall, the survey highlights the need to improve understanding of proper asthma control, especially since 33% of respondents reported missing school, work, or other social activities due to their asthma. To learn more, visit the Canadian Lung Association website at <https://www.lung.ca/news/latest-news/survey-asthma-not-well-controlled-most-canadians>.

Characterizing clients' verbal statements in behavioural support interventions: The case of smoking cessation

A study conducted by a professor from the University of British Columbia—and published in the *British Journal of Health Psychology*—examined conversations that smoking cessation counsellors in the United Kingdom had with clients trying to quit. Findings include that half of the statements that related to quitting mainly focused on medical aids like smoking cessation drugs, nicotine patches, and inhalers. Interestingly, the study also found that 50% of statements made by smokers had nothing to do with quitting even though the counselling sessions are designed to help them quit. The researcher thinks that these findings may indicate that smokers trying to quit need time to talk about a range of topics to then feel comfortable talking about smoking. To learn more, visit the University of British Columbia website at <https://news.ok.ubc.ca/2016/10/25/people-trying-to-quit-smoking-dont-always-focus-on-tobacco-cessation/>.

GSC's Health Management Support

Help your plan members get the support they need to take their medications—such as asthma medications—properly. Encourage them to sign up for Stick2It medication reminders on the Change4Life health portal via GSC's Plan Member Online Services.

And if you have plan members who want to quit smoking, spread the word about GSC's pharmacist-delivered counselling program for smoking cessation. As a customized intervention that is based on specific needs, plan members can choose counselling only, drug therapy only, or a combination of counselling and drug therapy.

Check with your GSC account team today!

COMMUNITY GIVING PROGRAM

HERE'S HOW WE ADD TO THE GREATER GOOD...



Paving the way for a brighter future

Take a look at how our grant recipients are making a difference

Frontline care—like dental services, vision care, prescription drugs, disease management, and mental health supports—can act as a catalyst for change. That's why the GSC Community Giving Program is focused on supporting organizations and initiatives that provide frontline care for underinsured or uninsured populations. And all grant recipients include a navigator component—this means ongoing positive change as clients are referred to any additional services they may need.

Frontline care in action

Jubilation Residential Centres Inc. — Prince Albert Seniors Advocacy Centre

For over 25 years, Jubilation has been helping young women, young parents with children, and socially stigmatized individuals and families living in Prince Albert and surrounding area in Saskatchewan, via a wide range of services and programs. For instance, the Centre is helping tackle homelessness through a joint project with the North Saskatchewan River Metis Local #269. Likewise, recognizing that seniors are a growing population—and one that often suffers the negative effects of social stigmatization—the Centre considers seniors a vulnerable population and is committed to making a difference in their lives.

A lifeline for seniors

Prince Albert is the service hub for people living throughout Northern Saskatchewan and, as Canada's population continues to age, the region is increasingly made up of seniors. Many seniors in the region are lower income, over 65 years old, and in a lot of cases, could be considered the "frail" elderly. Accordingly, in 2014, to address the needs of the growing seniors' population, Jubilation launched the Prince Albert Seniors Advocacy Centre.

Working with a team of volunteers—who themselves are seniors and very familiar with the region's health and social services—the Centre provides services out of its office, as well as via home visits. A main emphasis is helping seniors navigate the health care system not only to access basic care, but also to receive quality care. Navigation is also essential in helping seniors with complex issues like the provision of essential dental care that is affordable or ideally free.

The Centre also helps address social isolation, mental health issues, and elder abuse. Income security is another priority area as its ripple effect creates many physical and psychological challenges for seniors. In addition, in the bigger picture, the Centre has put into place a range of services aimed at health promotion and disease management, and it advocates with all levels of government regarding seniors' issues.

Laying down long-term roots

As the Centre continues to establish itself as a mainstay for helping seniors in the community, it continues to work towards its goal of becoming completely self-sustainable. Essential core funding from GSC is making it possible for the Centre to continue to help seniors while it builds a model for the future that is based on stable funding. Initiatives like fundraising and volunteer recruitment will become part of the strategy. To learn more, please visit the program's Facebook page at <https://www.facebook.com/paseniors>.

OUT & ABOUT... *An event not to miss*

2016 Mental Health Summit Vancouver – December 13, 2016

Fairmont Hotel, Vancouver, B.C.

<http://www.benefitscanada.com/conferences/mental-health-summit-vancouver>

GSC's Innovation Leader for Health Management, Peter Gove, will speak about "The Medicalization of Unhappiness."

GSC CUSTOMER SERVICE CENTRE 2016 HOLIDAY HOURS

Monday, December 26	CLOSED
Tuesday, December 27	CLOSED
Wednesday, December 28	8:30 a.m. to 8:30 p.m. EST
Thursday, December 29	8:30 a.m. to 8:30 p.m. EST
Friday, December 30	8:30 a.m. to 8:30 p.m. EST
Monday, January 2	CLOSED

Our regular business hours (8:30 a.m. to 8:30 p.m. ET) resume on Tuesday, January 3, 2017.

*December
Haiku*

Turn and face the change
Our plans have a chance to save
And still promote health

★ *Best wishes for a happy
and healthy 2017!* ★

WINNER OF THE DRAW FOR A FITBIT

Congratulations to **CAROL CHAGNON**, of **Hamilton, ON**, the winner of our monthly draw for a Fitbit. Through this contest, one name will be drawn each month from plan members who have registered for Plan Member Online Services for that month.



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London	1.800.265.4429	Vancouver	1.800.665.1494
Toronto	1.800.268.6613	Windsor	1.800.265.5615
Calgary	1.888.962.8533	Montréal	1.855.789.9214
	Customer Service		1.888.711.1119