Perspectives | Spring 2020

The Drug Pipeline:

What private plans can expect in 2020.

TELUS Health

Contents

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Introduction

Health Canada is currently reviewing more than 130 drug submissions; about half are for new drugs, and half are supplemental (that is, new indications for drugs already on the market). Perhaps the single-most newsworthy submission is one for a gene therapy—Canada's first. Used to treat a rare eye disorder, the cost would be about $1 million for both eyes.

Otherwise, as in previous years, cancer treatments lead the way among the submissions, accounting for about a quarter at this time. Most of these cancer therapies will be administered in a hospital, in which case private drug plans are not involved with coverage. However, one cancer drug, available in a capsule format, has the potential to significantly impact private plans, with an anticipated annual cost of more than $250,000.

This article further examines five new drug submissions deemed most likely to have an impact on private plans. One represents the continued evolution of second-line therapy for people with diabetes who may be struggling to manage their condition; another promises to be a breakthrough treatment for people with treatment-resistant depression.

Also included in this report are updates on what's happening in biosimilars (where developments are essentially in a holding pattern) and in generics (where there are many developments, though with limited cost-savings for private drug plans).

What to expect for:

Luxturna for a rare eye disorder.

If approved by Health Canada, Luxturna (generic name: voretigene neparvovec) will be the first gene therapy in Canada. The regulatory body received the submission in December 2019. Typically, this would lead to a decision in late 2020; however, Health Canada may take more time for the first gene therapy submission.

Approved by the U.S. Food and Drug Administration (FDA) in December 2017, the therapy treats a very rare, inherited eye disorder that typically leads to blindness. The FDA estimated a patient population of 1,000 to 2,000 Americans; if we assume a 10 to one ratio, that suggests an estimated Canadian population of 100 to 200.

In the U.S., the list price is US$425,000 per eye. The manufacturer has laid out, in the U.S. and in other markets, possible payment models, including outcomes-based arrangements and payment schedules that would span multiple years.

The funding for gene therapies in Canada is not yet clear. If administered in hospital, it should be publicly funded, but there may be pressure on private payers as well. In the case of Luxturna, which is injected into the eye, patients go to designated treatment centres, which meet the requirements for proper storage and administration.

Rybelsus for diabetes.

Analysts predict that Rybelsus (semaglutide) could be one of the top-five product launches of 2019 in the U.S., with forecasted global sales of $3 to $5 billion by 2024. The drug is currently under review by Health Canada, and TELUS Health expects it will be approved by June 2020.

What sets Rybelsus apart is the fact that it is the world's first oral tablet for a drug class that can significantly improve control of blood sugar levels for people with type 2 diabetes. The drug class is GLP-1 RAs (glucon-like protein-1 receptor agonists). Until now, these drugs have been injectable only. GLP-1 RAs are prescribed as a second-line therapy for patients whose blood sugar levels remain above recommended targets despite the use of metformin, the recommended first line of therapy, and despite efforts to make lifestyle changes (i.e., improved diet and activity levels).

TELUS Health claims data report that total eligible costs for GLP-1 RA claims increased from $24.4 million in 2014 to $48 million in 2018. The average cost per claimant per year is about $2,000, compared to less than $100 for metformin.

In clinical studies, Rybelsus outperformed other oral drugs that are second-line therapies for type 2 diabetes. Prescribing may also increase following a new clinical guideline in the U.S., which recommends that a second-line therapy, such as a GLP-1 RA, be prescribed for patients at high risk of cardiovascular disease or chronic kidney disease, even if their blood sugar levels are at target. Canadian clinical guidelines will likely follow suit.

The list price for Rybelsus has yet to be announced in Canada. TELUS Health estimates a cost of $2,000 to $2,500 per year, comparable to the injectable format (brand name: Ozempic).

More than 2 million Canadians (7.3%) have diabetes, according to Statistics Canada. The majority (90% to 95%) have type 2 diabetes. Diabetes management can be a challenge: studies in Canada and around the world consistently show that less than half of type 2 diabetes patients are able to maintain blood sugar levels at recommended target levels[1].

Spravato, a nasal spray for depression.

Health Canada is reviewing Spravato (esketamine hydrochloride) under its priority review policy in order to render a quicker decision; approval is expected early in 2020. The drug is intended for patients with treatment-resistant depression, who have tried at least two other antidepressants without adequate results. It is also indicated for people who are suicidal.

Traditional antidepressants take eight to 10 weeks to be effective. Spravato, a nasal spray, works within hours. It is also available by injection, although that format is not part of the current Health Canada review.

In Canada, about 11% of the population (four million) has reported at least one episode of major depressive disorder in their lifetime. Between 10% and 30% of these patients are subsequently diagnosed as treatment resistant. Roughly speaking, between 400,000 and 1.2 million Canadians may be candidates for treatment with Spravato. It would be used in combination with an oral antidepressant.

The FDA approved Spravato in September 2019. However, the risk of serious outcomes and potential for abuse—the drug is related to ketamine, which is used as an anesthetic—requires that the drug be available with strict conditions. Patients must self-administer the spray in a healthcare provider's office and cannot take the product home. The patient must be monitored by the healthcare provider for two hours and should not drive or operate heavy machinery for the rest of the day.

The cost of Spravato in Canada is unknown at this time. In the U.S., the expected annual cost, based on list price, is between US$33,000 and $49,000.

[1] Khunti K, Ceriello A, Cos X, et al. Achievement of guideline targets for blood pressure, lipid, and glycaemic control in type 2 diabetes: A meta-analysis. Diabetes Res Clin Pract. 2018 Mar 137:137-48.

Rozlytrek for rare cancers.

Rozlytrek (entrectinib) recently became Canada's second cancer drug that targets tumours based on certain genetic properties, regardless of where the tumour is in the body. These tumour-agnostic drugs are considered a breakthrough in therapy for rare cancers, which often test positive for the target genes. Clinical studies show a positive durable response of more than two years for a significant number of patients with locally advanced (i.e., can't be surgically removed) or metastatic cancers.

Health Canada approved Rozlytrek in February 2020. It approved the first tumour-agnostic drug, Vitrakvi, in July 2019.

Both Rozlytrek and Vitrakvi are produced in capsule format, which means that private drug plans are more likely to be the first payer, rather than hospitals or public plans. At the time of publication of this article, pricing for Rozlytrek was not yet known. It is expected to be comparable to Vitrakvi, which costs between CDN$18,000 and $24,000 per 28-day cycle, or approximately $234,000 to $312,000 per year, according to pricing provided to the pan-Canadian Oncology Drug Review.

Reimbursement decisions for this new class of tumour-agnostic cancer drugs are especially challenging and complex, given the variances in cost based on tumour type as well as the variances in comparator drugs for each tumour type.

Each year, in the U.S., an estimated 2,500 to 3,000 people develop cancers that meet the criteria for these drugs. That translates into roughly 250 to 300 people here in Canada.

Xofluza for influenza.

Xofluza (baloxavir marboxil) recently became the second antiviral drug to treat influenza, approved by Health Canada in February 2020 and more than two decades after the arrival of the first flu antiviral, Tamiflu.

Unlike Tamiflu, which must be taken twice a day for five days, Xofluza requires a single dose of two tablets. It can provide relief from flu symptoms after just 26 hours and can be taken by children aged 12 and older. Both must be taken with 48 hours of initial symptoms.

The FDA approved Xofluza in October 2018. The U.S. list price is US$150, comparable to the cost of Tamiflu. Xofluza's Canadian price has yet to be announced; generic Tamiflu (oseltamivir), meanwhile, can be purchased for about $25 per treatment cycle.

In Canada, the Public Health Agency of Canada estimates that an average of 3.5 million people are ill with influenza each year, resulting in more than 12,000 hospitalizations and approximately 3,500 deaths.

Rinvoq for inflammatory disease.

Health Canada approved the first indication for Rinvoq (upadacitinib) in January 2020, for rheumatoid arthritis (RA). Rinvoq is not a biologic and comes in a pill format. While this approval will not likely impact private drug plans much, given that it is priced in line with other similar oral medications for RA, expected approvals for the other indications in the coming years will likely have an effect.

In the future, Rinvoq may also be approved to treat other conditions such as Crohn's disease, ankylosing spondylitis, ulcerative colitis, atopic dermatitis, psoriatic arthritis and juvenile idiopathic arthritis. Its availability for these conditions will likely expand claimant pools. The cost impact in these other indications will depend on the cost of other comparator drugs at the time of approval.

Stendra for erectile dysfunction.

The category for erectile dysfunction (ED) drugs is already heavily genericized. However, the market may see a small uptick with the release of Stendra (avanafil) since it is a second-generation ED drug that is being advertised as faster-acting with fewer side effects than the first-generation drugs.

Health Canada approval will likely occur in the third quarter of 2020. In the U.S., Stendra has been available since 2012, at a list price of about US$68 per tablet. In Canada, generic Viagra (sildenafil) is available for about $9 per pill.

ED affects an estimated 3 million Canadian men over the age of 40 (49%). Research has also shown that ED may be associated with cardiovascular disease.

Table 1

Drug name	Disease/ indication	Drug format	Anticipated timing	Estimated cost*
Luxturna	Rare eye disorder	Injection into eye	Health Canada review initiated Dec. 2019; approval expected in late 2020	$565,000 per eye *
Rybelsus	Diabetes	Oral tablet	Health Canada review initiated Oct. 2019; approval expected by June 2020	$2,000 - $2,500 annually
Spravato	Depression	Nasal spray	Health Canada review initiated Jan. 2019; approval expected Q1 2020	$43,800 - $65,000 annually *
Rozlytrek	Non-site-specific cancer tumours	Oral capsule	Health Canada review initiated June 2019; approval expected Q1 2020	$234,000 - $312,000 annually
Xofluza	Influenza	Oral tablet	Health Canada review initiated May 2019; approval expected Q2 2020	$200 for a single treatment
Rinvoq	Rheumatoid arthritis	Oral tablet	Approved by Health Canada in Jan. 2020	$78,400 annually *
Stendra	Erectile dysfunction	Oral tablet	Health Canada review initiated June 2019; approval expected Q3 2020	$90 per tablet *

*Based on list-price information in the U.S., converted to Canadian dollars.

Biosimilars

For the second year in a row, private drug plans will not likely see any new biosimilars enter the market. This is in contrast to public plans, which anticipate a number of biosimilar oncology drugs.

Behind the scenes on the private side, however, a bottleneck is building for biosimilar versions of Humira (adalimumab), used to treat rheumatoid arthritis and other autoimmune conditions. Health Canada approved the first adalimumab biosimilar (Hadlima) in May 2018, and three additional adalimumab biosimilars are in the queue at Health Canada. However, litigation has delayed the launch of Hadlima and will likely delay the launch of all four biosimilars until at least 2021.

When they finally launch, the impact on private plans is uncertain. Humira is one of five originator biologics that are referred to as anti-TNF (tumour necrosis factor) drugs, and four anti-TNF biosimilars are already available in Canada. The biosimilars for Humira will bring the total to eight, resulting in a relatively crowded market where uptake so far has been low. The TELUS Health 2019 Drug Data & National Benchmarks report indicates that Inflectra, the first anti-TNF biosimilar, captured just 8% of new claimants and 4% of eligible costs in 2018.

Reimbursement policies may, however, kickstart the greater use of biosimilars. Public plans in B.C. and Alberta were the first to implement policies that require patients to switch to a biosimilar if they wish to continue to receive coverage; time will tell whether other provinces, and private insurers, will follow.

Table 2 summarizes what's coming in biosimilars for private drug plans.

Table 2

Biosimilar name	Brand name (reference drug)	Disease/indication	Anticipated timing	Estimated cost of biosimilar*
Hadlima	Humira (adalimumab)	Rheumatoid arthritis and other autoimmune conditions	Approved by Health Canada in May 2018; litigation will likely delay launch until 2021	$13,100 - $15,000, based on indication and dosage requirements
Hyrimoz	Humira (adalimumab)	Rheumatoid arthritis and other autoimmune conditions	Health Canada review initiated Nov. 2018	$13,100 - $15,000, based on indication and dosage requirements
Hulio	Humira (adalimumab)	Rheumatoid arthritis and other autoimmune conditions	Health Canada review initiated Sept. 2019	$13,100 - $15,000, based on indication and dosage requirements
Idacio	Humira (adalimumab)	Rheumatoid arthritis and other autoimmune conditions	Health Canada review initiated Oct. 2019	$13,100 - $15,000, based on indication and dosage requirements

*Based on a list price that is 20% to 30% lower than originator biologic's list price, calculated as an average across five indications (RA, ulcerative colitis, psoriasis, Crohn's disease and ankylosing spondylitis), per reporting by CADTH (Canadian Agency for Drugs and Technologies in Health).

Generics

Compared to 2019, when just a handful of generic launches impacted private drug plans, 2020 will see many arrivals on the generics front. However, cost savings will not be noticeable in most cases. This year's generic drugs are indicated for small patient populations or join categories that are already heavily genericized.

The next two to three years will likely see greater savings for private plans, due to generics in two very different categories: diabetes and multiple sclerosis. The first generics for a second-line therapy for diabetes are expected to arrive in 2021 or 2022, depending on the resolution of patent litigations. The reference brand-name drugs cost about $800 to $1,200 annually.

The first of four generics for multiple sclerosis (MS) entered the market in October 2019. Another three generics for MS are expected over the next three years, pending litigation. Costs for the original brand-name drugs range from $20,000 to $40,000 per year.

Table 3 summarizes what private drug plans can expect in the generics arena over the next few years, in order of anticipated market launch.

Table 3

Generic name	Brand name(s) (reference drug)	Disease/indication	Anticipated entry in market
Tacrolimus	Advagraf	Immunosuppressive following organ transplant;	Q1 2020 probable
Prucalopride succinate	Resotran,	Chronic constipation	Q1 2020 probable
Cabazitaxel	Jevtana	Prostate cancer	Q1 2020 probable
Plerixafor	Mozobil	Stem cell transplant for non-Hodgkin's lymphoma and multiple myeloma	Q1 2020 possible; however, litigation expected
Fampridine	Fampyra	Multiple sclerosis	Feb. 2020 possible, pending litigation
Dasatinib	Sprycel	Leukemia	April 2020 possible; litigation close to completion
Dienogest	Visanne	Endometriosis	April 2020 possible
Carbidopa, entacapone, levodopa	Lodosyn, Stalevo, Comtan	Parkinson's disease	June 2020 possible
Apixaban	Eliquis	Anticoagulant (prevention of blood clots)	June 2020 possible, pending litigation
Ruxolitinib phosphate	Jakavi	Bone cancer	June 2020 possible, pending litigation
Orlistat	Xenical	Obesity	Sept. 2020 possible
Pirfenidone	Esbriet	Idiopathic pulmonary fibrosis (lung disease)	Oct. 2020 possible; however, litigation expected
Colesevelam hydrochloride	Lodalis	High cholesterol	Q3 2020 probable
Fesoterodine	Toviaz	Overactive bladder syndrome	Nov. 2020 possible; however, litigation expected
Nebivolol hydrochloride	Bystolic	Hypertension	Dec. 2020 probable
Rivaroxaban	Xarelto	Anticoagulant (to prevent blood clots)	Dec. 2020 possible, pending litigation
Saxagliptin	Onglyza	Diabetes	March 2021 possible, pending litigation
Dimethyl fumarate	Tecfidera	Multiple sclerosis	Oct. 2021 possible, pending litigation
Linagliptin	Trajenta	Diabetes	Feb. 2022 possible, pending litigation
Terflunomide	Aubagio	Multiple sclerosis	May 2022 possible, pending litigation

On the horizon

Here is an advance look at a few possible breakthrough drugs that may—or may not—enter Canada's drug pipeline in the near future.

Multiple sclerosis

The U.S. Food and Drug Administration (FDA) initially declined to review Ozanimod in early 2018 due to insufficient data. The manufacturer (Celgene) regrouped and produced results from two clinical trials, and both the FDA and European Medicines Agency accepted applications for Ozanimod in June 2019. A submission to Health Canada is expected. The drug uses a novel mechanism of action and its oral format may be preferred over injectable alternatives. The estimated annual cost is $20,000 or more.

Early Alzheimer's disease

This is the second time around for a new biologic drug containing aducanumab (brand name to be announced). The manufacturer, Biogen, stopped development in March 2019 after a preliminary analysis of clinical trials fell short of expectations. However, a subsequent analysis, with three more months of data and focussed on participants receiving higher doses, showed positive findings. Biogen has resumed development of the drug, working closely with the FDA, though it's not known when the drug will be ready to submit for review. Given that the drug is intended for those with early Alzheimer's, which typically begins when a person is in their 50s, this biologic would have a cost impact on private plans. Pricing has yet to be determined. This would be the first new, and possibly breakthrough, treatment for Alzheimer's in nearly 20 years.

Peanut allergy

The FDA approved the world's first drug to prevent severe allergic reactions in early 2020. Palforzia is an oral biologic that gradually desensitizes the body to the allergen and inhibits the allergic reaction. It will not eliminate the allergy, but it will enable people to tolerate accidental exposure to small amounts of peanut, thereby preventing anaphylaxis (a life-threatening reaction) and trips to the emergency department. It is not known when or if Palforzia will be submitted to Health Canada. Its cost is also unknown at this time.

Spinal muscular atrophy

Zolgensma is a gene therapy, indicated for spinal muscular atrophy (SMA) in children up to two years old. SMA is the leading genetic cause of death in infants; those who live beyond two years progressively lose motor function and may require a ventilator to breathe. The FDA approved Zolgensma in May 2019, and more than 100 infants were treated in the first three months of availability. The one-time cost is US$2.1 million per patient. Novartis, the manufacturer, recently began to offer 100 free doses a year by way of a global lottery, with random selections made every two weeks.

While it's not known whether Zolgensma will be submitted to Health Canada for review, another treatment for SMA, called Spinraza, was approved in July 2017. The estimated cost of Spinraza, which can be used by adults as well as children, is $700,000 in year one and $300,000 annually in subsequent years, for the lifetime of the patient.

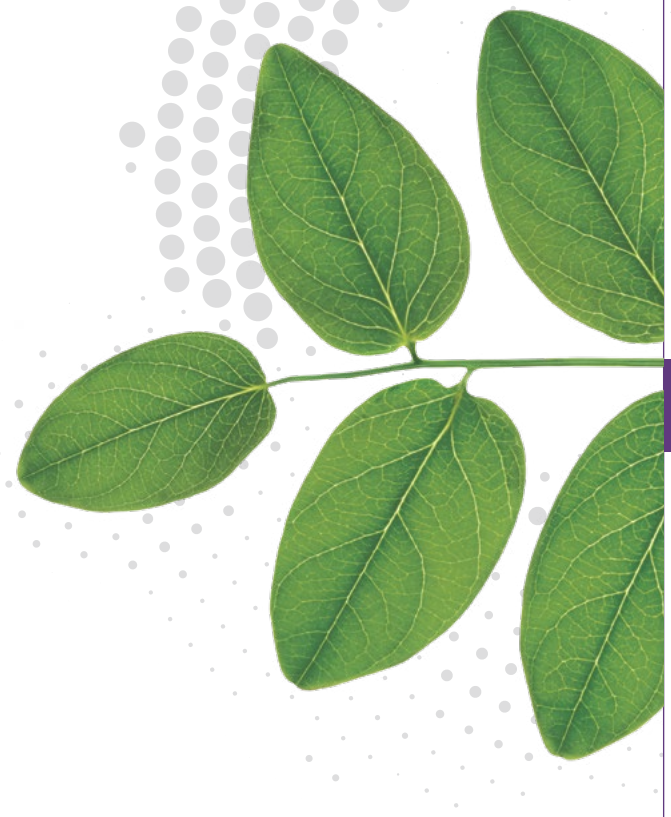
What happens after the pipeline?

Check out the TELUS Health report entitled, The Drug Pipeline: Whatever happened to? Drawing from TELUS Health's database of more than 12 million privately insured Canadians, the report gives a detailed update on the impact of new, therapeutically significant drugs in five categories: cancer, cholesterol, migraine, hepatitis and weight management.

Conclusion

Compared to recent years, Canada's drug pipeline for private drug plans can be described as relatively quiet in 2020. The two most anticipated launches are in the areas of diabetes and depression. Both drugs deliver therapeutic value, given their solid clinical results for patients who appear to be struggling to manage their condition despite efforts to use existing treatments. Canada's first gene therapy is also on the horizon, with a possible launch in late 2020 or early 2021.

This year's report also underscores that in Canada and around the world, we are firmly in the "new normal" of medical research, where the focus is on breakthrough or novel advances in treatment for well-defined patient populations. As well, a growing proportion of these new drugs will be available as a pill or by self-injection, which means that private drug plans will likely be the first payer, rather than hospitals. While most of the resulting drugs come with much higher prices, or are relatively costly compared to existing treatments, their potential to offset downstream costs—such as disability leaves and hospitalizations—spurs continued innovation, as well as evolution in the areas of market access, plan design and reimbursement policies.



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