Perspectives | Spring 2021

The Drug Pipeline:
What private plans can expect in 2021.

TELUS Health

Contents

Mark Jackson, BScPhm, RPh
Consultant Pharmacist, TELUS Health

Introduction

Currently, Health Canada is reviewing more than 150 drug submissions, compared to about 130 at this time last year. Just over half of today's submissions (89) are for new drugs; the remainder are supplemental submissions (that is, new indications for drugs already on the market). Treatments for COVID-19 are among those submissions; however, just one, colchicine, would have an impact on private drug plans (the rest would be publicly funded, at least for the foreseeable future).

As in past years, cancer therapies account for the largest share of new drug submissions, at 35%. This year, however, none are expected to have a major impact on private drug plans.

In other drug categories, TELUS Health has identified three new drugs that could significantly affect private plans. One is a new option to treat acute migraine, which affects more than 3 million Canadians. The other two treat rare diseases: one for spinal muscular atrophy and the other for cystic fibrosis. This article also examines the potential impact of colchicine, a possible treatment for COVID-19, and six other drug submissions of interest to private drug plans.

In the biosimilars space, six biosimilar options are expected for Humira, a reference biologic that ranks second in eligible costs for private drug plans. Also included in this report are summaries of what to expect for generics in 2021, plus a look at what likely lies on the horizon for Canada's drug pipeline.

What to expect for:

COVID-19

As of late March, Health Canada had accepted 12 products for review for the prevention or treatment of COVID-19. Six are vaccines, of which four have been approved. Among the remaining six products, private plans may eventually see claims for just one of them: colchicine.

Health Canada is reviewing colchicine as a potential treatment for ambulatory patients with moderate to severe COVID-19. As a genericized drug that's long been available to treat gout, it sells for less than $1 per tablet for that indication. However, results from clinical trials for its use against COVID-19 have generated debate among researchers and practitioners. Given Health Canada's fast-tracking of reviews for COVID-19 submissions, a decision is expected by June 2021 at the latest.

Another treatment is worth mention: bamlanivimab, approved by Health Canada in November 2020. It is indicated for the treatment of mild to moderate COVID-19 for people aged 12 and older who are at high risk of progressing to severe illness and hospitalization. A biologic, it is administered as a single infusion as soon as possible after a positive test of COVID and within 10 days of the onset of symptoms. A similar biologic therapy—a combination of casirivimab and imdevimab—is under review.

Funding for bamlanivimab is federal at this point: the government has purchased 26,000 doses at a cost of US$32.5 million (US$1,250 per dose). Time will tell if coverage eventually transfers to provincial plans—and possibly private plans, if this infectious disease persists and administration expands outside of hospitals.

Migraine

About 3.1 million Canadians today suffer from migraine headaches, based on an estimated prevalence rate of 8.3%.[1] Drugs in the triptan category are the go-to treatment for acute migraines, and generic versions of all triptans have been available for some time. The average cost of a generic triptan is $10 or less per tablet.

Reyvow (generic name: lasmiditan) from Eli Lilly will be the first new drug for acute migraine since the launch of triptans almost 30 years ago. It has a new mechanism of action that will make it a welcome option for treatment. In the U.S., where the Food and Drug Administration (FDA) approved the drug in October 2019, the list price is about US$80 per tablet.

Health Canada began its review of Reyvow in April 2020 and approval will likely occur by June this year. If used as a first line of therapy, replacing triptans, its impact on private plans could well be high given the difference in price. If its use is reserved for those not responding to triptans, the impact will likely be low.

Spinal muscular atrophy

If approved, Evrysdi (risdiplam) from Hoffmann-La Roche will become the third ground-breaking therapy available for spinal muscular atrophy (SMA), a rare disease that is the leading genetic cause of death in infants. Children with this disease who live beyond two years progressively lose motor function and may require a ventilator to breathe. The Canadian Paediatric Surveillance Program estimates 35 new cases of SMA per year in Canada.[2]

Evrysdi would be the first oral treatment option for SMA. Zolgensma, a gene therapy (approved by Health Canada in December 2020), is administered by intravenous infusion, and Spinraza (approved in 2017) is administered by injection into the spinal canal.

As an oral solution that does not require administration in a clinical setting, Evrysdi may significantly impact private drug plans. While the list price in Canada has yet to be announced, the average annual price in the U.S. ranges from US$100,000 to a maximum of US$340,000.

By comparison, Spinraza's list price in Canada is $708,000 for the first year of treatment and $354,000 annually in subsequent years. The price of Zolgensma, a one-time treatment, is about $2.8 million in Canada.

Evrysdi, like Spinraza, can be used by children and adults, while Zolgensma is indicated for the pediatric population only. The use of Zolgensma will likely focus on the youngest of patients, who will experience the most significant results in terms of halting the disease, while older patients would use Spinraza or Evrysdi—and perhaps more likely Evrysdi, given its oral format and lower price tag.

Cystic fibrosis

While the category is getting crowded, the new drug Trikafta has been described as a "game changer" for the treatment of cystic fibrosis (CF) for two reasons:

1. As a triple combination therapy (containing ivacaftor, tezacaftor and elexacaftor), it has demonstrated significant improvements in health outcomes; and
2. It can potentially treat up to 90% of the patient population whereas other medications typically target fewer than 10%, depending on the genetic mutation of the CF.

Cystic Fibrosis Canada describes Trikafta, an oral medication, as the "single biggest advancement in treating cystic fibrosis in the history of the disease." It is advocating for its approval in Canada, with funding from public drug plans.

[1] Ramage-Morin PL, Gilmore H. Prevalence of migraine in the Canadian household population. Health Rep. 2014 Jun;25(6):10.6. https://pubmed.ncbi.nlm.nih.gov/24941316/ (Accessed March 2021) [2] Mah JK, Haig T, Hodgkinson V, et al. 5q spinal muscular atrophy: study protocols. Canadian Paediatric Surveillance Program. https://www.cpsp.cps.ca/uploads/studies/5q-spinal-muscular-atrophy-protocol.pdf (Accessed March 2021)

The FDA approved Trikafta, manufactured by Vertex Pharmaceuticals, in October 2019 after designating it a break-through therapy and fast-tracking its review. Its list price is US$311,000 annually.

In Canada, Health Canada began its review of Trikafta in December 2020 under its Priority Review Policy, which has an accelerated target timeline of 180 days (six months).

CF is a rare genetic disease affecting approximately one in every 3,600 children born in Canada. Based on the Canadian Cystic Fibrosis Registry, more than 4,300 Canadians live with the disease. The median age of survival is 54.3 years.

High cholesterol

Health Canada began its review of Leqvio (inclisiran), manufactured by Novartis Pharmaceuticals, in September 2020. It would be the first entry in a new category of cholesterol medications known as small interfering RNA (siRNA). It will be used in a similar fashion to the PCSK9 inhibitors, Repatha (launched in 2015) and Praluent (2016).

PCSK9s are a second-line therapy for people who have cholesterol disorders due to a certain genetic condition or who also have heart disease, and who are unable to bring their cholesterol down to target levels despite taking first-line statin drugs. The list price for Repatha and Praluent is between $7,000 and $9,000; however, fewer than half of one per cent of claimants used a PCSK9, according to TELUS Health claims data (for more information on the impact of PCSK9s, see the TELUS Health report, The Drug Pipeline: Whatever Happened To?).

What sets Leqvio apart is the fact that it is administered by injection just twice a year, by a healthcare professional, whereas Repatha and Praluent are administered by self-injection every two or four weeks. Leqvio's low frequency of dosing may make it more appealing to patients.

However, Leqvio hit a roadblock in the U.S. in December 2020 when the FDA chose not to approve the drug due to "unresolved facility inspection-related conditions" involving a European manufacturing facility. If the FDA determines that an onsite inspection is required, it would be scheduled once safe travel is resumed. Even if the FDA's conditions can be met without onsite inspection, it might be 2022 before the drug is approved south of the border.

Time will soon tell if Health Canada makes similar decisions. The application for Leqvio is currently part of Health Canada's aligned review process, which gets products to market sooner by reducing the time lag between Health Canada's approval and recommendations for coverage from Canada's health technology assessment organizations (the Canadian Agency for Drugs and Technologies in Health and, in Quebec, l'Institut national d'excellence en santé et en services sociaux).

Meanwhile, the European Commission approved Leqvio in December 2020. The list price has yet to be announced, although it's expected to be similar to that of Repatha and Praluent.

Multiple sclerosis

While the patient population for multiple sclerosis (MS) is small, affecting approximately 77,000 Canadians today,[3] MS drugs ranked eighth on the list of top 10 drug categories by eligible cost in 2019, according to the 2020 TELUS Health Drug Data Trends & National Benchmarks report. The latest three entries, one of them a biologic, bring the category's total count of drugs to 19.

Health Canada approved Kesimpta (ofatumumab) in January 2021, less than a year after submission by Novartis Pharmaceuticals in May 2020. The list price is between $33,000 and $35,000 in the drug's first year of use, then about $28,000 annually.

[3] Multiple sclerosis in Canada (infographic). Canadian Chronic Disease Surveillance System. 2018 March. https://www.canada.ca/content/dam/phac-aspc/documents/services/publications/diseases-conditions/multiple-sclerosis-infographic/multiple-sclerosis-infographic.pdf (Accessed February 2020)

Kesimpta, a biologic, is similar to Ocrevus (ocrelizumab). Since Ocrevus's launch four years ago, it has become the top MS drug by eligible costs. TELUS Health claims data for 2020 found that the average annual eligible cost per claimant for Ocrevus was close to $26,000, compared to about $19,000 for the category overall.

Vumerity (diroximel fumarate) is a good example of product life cycle management on the part of its manufacturer, Biogen Canada. It is expected to become available soon after the patent expires for Tecfidera, Biogen's other drug for MS. Vumerity is very similar to Tecfidera—in fact, it is considered bioequivalent—although its formulation has been improved to reduce the likelihood of gastrointestinal side effects.

Health Canada accepted Biogen's application for the review of Vumerity in July 2020. In the U.S., the FDA approved Vumerity in October 2020. The expected list price in Canada will be $23,000 per year, in line with pricing for Tecfidera.

The brand name for ponesimod, the third new drug expected for MS this year, has yet to be announced by its manufacturer, Janssen. Health Canada began its review in July 2020 and approval is expected by June 2021. Its estimated list price will be around $30,000 annually.

More information on the evolution of the MS drug category and its impact on private drug plans can be found in the TELUS Health 2021 Category Watch: The Impact of New Drugs report.

Wilson disease

Wilson disease is a rare hereditary condition. The Canadian Liver Foundation estimates it affects one in every 30,000 Canadians, resulting in a patient population of about 1,250 today. Left untreated, the disease can be fatal. Fortunately, the majority of patients respond well to treatment with a drug that has long been available as a generic in Canada, at a cost of about $3,000 to $7,300 annually.

However, up to 40% of Canadians with Wilson disease cannot tolerate this medication and may need trientine, available as a generic drug.[4] Until recently, patients had to go through Health Canada's special access program (SAP) to purchase trientine. Under the SAP, drugs not marketed in Canada can be imported directly from another country (typically from the U.S.). The list price of trientine is about US$18,275 for 100 capsules, which translates into US$133,400 to US$333,500 annually.

Private plans are under no obligation to cover SAP drugs since they have not been approved by Health Canada. However, Health Canada has opted to pull trientine out of the SAP and regulate it as it does other drugs, using a special review process. In September 2020 it approved one generic version of the drug, and another review is underway. The change in approach removes significant administrative work from Health Canada and prescribers; however, it places coverage of this high-cost drug firmly into the private sphere.

Dayvigo for insomnia

The prevalence of insomnia is high, affecting 13.4% of the population (or about five million Canadians).[5] Dayvigo (lemborexant), manufactured by Eisai, may represent an important new treatment option, as its mechanism of action does not involve sedation, which sets it apart from all other insomnia drugs. However, its place in therapy will likely be after traditional agents, which are all available as lower-cost generics.

Health Canada approved Dayvigo in February 2021. While its average list price in Canada is not yet known, its price in the U.S. is about US$10 per tablet. In comparison, generic insomnia drugs are typically priced at less than $1 per tablet in Canada.

It will be interesting to see if Dayvigo fares better in Canada than Belsomra (suvorexant), which was discontinued for "business reasons" in May 2020, barely a year after its launch in April 2019. Like Dayvigo, it uses a non-sedative mechanism of action. It was approved by the FDA in December 2019 and remains available in the U.S.

[4] Chandok N, Roberts EA. The trientine crisis in Canada: A call to advocacy. Can J Gastroenterol Hepatol. 2014 Apr;28(4);184. [5] Morin CM, LeBlanc M, Bélanger L, et al. Prevalence of Insomnia and its treatment in Canada. Can J Psychiatry. 2011 Sep;56(9):540-8.

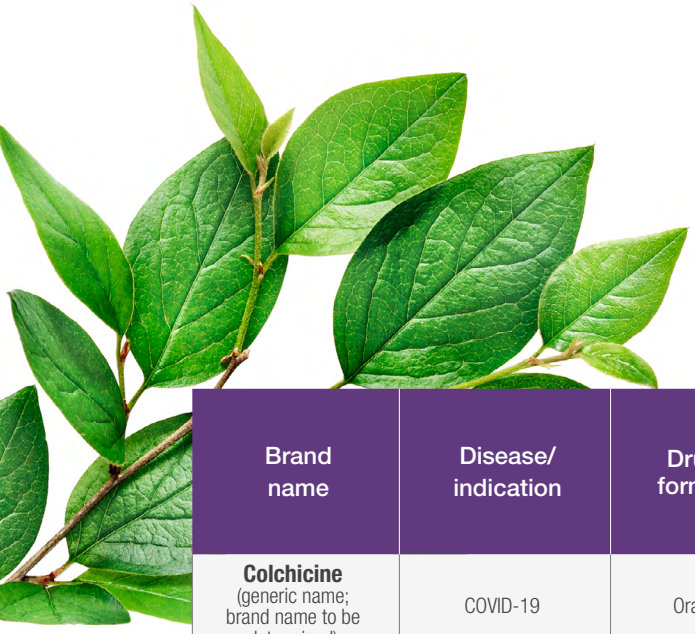

Table 1 – 2021 Drug pipeline summary

Brand name	Disease/ indication	Drug format	Health Canada review	Estimated list price	Potential impact on private plans
Colchicine (generic name; brand name to be determined)	COVID-19	Oral	Initiated January 2021; approval expected by June 2021	Unknown	Low
Dayvigo	Insomnia	Oral	Approved Feb. 2021	$13 per tablet*	Low
Evrysdi	Spinal muscular atrophy	Oral solution	Initiated Oct. 2020; under Priority Review; approval expected by March 2021	$127,000 to $433,000 annually*	High
Kesimpta	Multiple sclerosis	Self-injection	Approved Jan. 2021	$33,000- $35,000 in Year 1, then $28,000 annually	Medium
Leqvio	High cholesterol	Injection by healthcare provider	Initiated Sept. 2020; approval expected by Sept. 2021	$8,000 annually	Medium
Ponesimod (generic name; brand name to be determined)	Multiple sclerosis	Oral	Initiated July 2020; approval expected by June 2021	$30,000 annually	Medium
Reyvow	Acute migraine	Oral	Initiated April 2020; approval expected by June 2021	$100 per tablet*	High
Trientine (generic)	Wilson disease	Oral	One approved Sept. 2020; second under review	$170,000 to $425,000 annually*	Medium
Trikafta	Cystic fibrosis	Oral	Initiated Dec. 2020 under Priority Review; approval expected by June 2021	$396,000 annually*	High
Vumerity	Multiple sclerosis	Oral	Initiated July 2020; approval expected by June 2021	$23,000 annually	Medium

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

Biosimilars

A two-year drought of new biosimilars available for coverage by private plans is over: 2021 will likely see the launch of up to six biosimilar versions of Humira (adalimumab), which treats rheumatoid arthritis and other autoimmune conditions. Pricing negotiations with the pan-Canadian Pharmaceutical Alliance (pCPA), which set prices for both public and private plans, concluded in January 2021. The coming months will see provinces and territories finalize pricing for their respective jurisdictions.

Prices will vary based on the condition treated. Assuming an average price that is 20% to 30% lower than the reference biologic and that takes into account the multiple indications, the estimated annual cost for each of these six biosimilars is $12,000 to $17,000 (compared to $18,000 to $22,000 for Humira).

The six biosimilars for Humira join three biosimilars for Remicade (infliximab). For years, Remicade and Humira have been the top two drugs by eligible cost for private drug plans, according to TELUS Health claims data. Their biosimilar options therefore represent significant savings.

However, despite the availability of biosimilar options for Remicade for a number of years, uptake has been low—until now. Recent provincial switching policies have spurred the utilization of biosimilar biologics and will likely prompt the adoption of similar policies by private plans, as well as influence physicians' prescribing behaviour for all patients.

In May 2019, B.C. became the first jurisdiction to require patients to switch to a biosimilar if they wished to continue to receive coverage from the province's PharmaCare program. Alberta followed suit in November 2019, although COVID-19 interrupted implementation of its policy (which began to take effect in January 2021). In February 2020, Ontario announced it would implement a switching policy as well, though again COVID-19 delayed the release of details regarding implementation.

Outside of the biosimilars for Humira, no other biosimilars are in the current or near-term pipeline that would have a significant impact on private plans.

Table 2 – Biosimilars for Humira anticipated in 2021

Biosimilar brand name	Manufacturer
Amjevita	Amgen
Hadlima	Merck
Hulio	Viatris
Hyrimoz	Sandoz
Idacio	Fresenius Kabi
To be determined	Pfizer

Generics

Perhaps the most anticipated generic launch is for rivaroxaban, available under the brand name of Xarelto. The anticoagulant is used to treat or prevent blood clots, and physicians will welcome its availability as an alternative to warfarin, another generic anticoagulant that carries a higher risk of bleeding. As well, private and public payers will see strong savings since six generic rivaroxaban drugs are under review. If three or more are approved, pCPA's generic pricing policy dictates that their prices must be 25% of the brand-name price.

Health Canada approved the first generic for Xarelto in November 2020. However, litigation may delay its launch until late 2021 or later.

Other anticipated generic entries are in the diabetes category. Onglyza (saxagliptin) and Komboglyze (saxagliptin and metformin) are the first of 10 DPP-4 (dipeptidyl peptidase-4) inhibitors to go generic, although litigation may delay their launch until early 2022. This second line of therapy for people with type 2 diabetes represented 17.3% of eligible costs for the total diabetes category in TELUS Health's book of business in 2020. The average cost per claim was $159, compared to $23 per claim for metformin, the standard first line of therapy. Generic options for all 10 DPP-4s are expected over the next few years.

Approvals for eight generic options for Tecfidera, to treat MS, are expected by Fall 2021, with product launches soon after. Given the high number of generics and pCPA's pricing policy, the expected list price will be about $6,250 annually (i.e., 25% of Tecfidera's price of about $25,000). Generic alternatives for Fampyra (fampridine), another MS treatment, have already received approval but have yet to launch due to litigation.

The manufacturer of Tecfidera is also expected to launch a new MS drug—Vumerity, which is chemically related to Tecfidera—this year (see page 6).

Table 3 summarizes these and other generic drugs that are expected to launch in the next two years and that can be expected to have an impact on private drug plans.

Table 3 – New generic drugs, by date of market entry

Generic name	Brand name(s) (reference drug)	Disease/indication	Anticipated entry in market
Bendamustine hydrochloride	Treanda	Cancer	Q1 2021
Ticagrelor	Brilinta	Acute coronary syndrome/prevention of stroke, heart attack	May 2021, pending litigation
Tolvaptan	Samsca	Hyponatremia	June 2021
Treprostinil	Remodulin	Pulmonary arterial hypertension	June 2021
Fampridine	Fampyra	Multiple sclerosis	Generics approved May 2020, launches pending litigation
Dimethyl fumerate	Tecfidera	Multiple sclerosis	Oct. 2021
Efinaconazole	Jublia	Toenail fungus	Oct. 2021
Rivaroxaban	Xarelto	Treatment/prevention of blood clots	To be determined, pending litigation
Saxagliptin	Onglyza	Diabetes	Early 2022, pending litigation
Saxagliptin and metformin	Komboglyze	Diabetes	Early 2022, pending litigation

On the horizon

Here is a preview of drugs that may enter Canada's pipeline in the near future, that will be of interest to private drug plans.

Early Alzheimer's disease

A new biologic containing aducanumab (brand name to be determined) has had more than its share of ups and downs in the past few years. Since initial clinical trials failed in 2019, manufacturer Biogen refocused its efforts on a subset of patients with early disease who had experienced positive results, and has been working closely with the FDA to meet regulatory requirements. In January, the FDA announced it would need another three months (until June) to make its decision—which led to a jump in Biogen shares, because delays typically lead to approvals. If approved in the U.S., this drug will likely be submitted to Health Canada for review. Given that it is indicated for early Alzheimer's disease, which may begin when a person is in their 50s, this biologic would have a greater cost impact on private plans than previous drugs for Alzheimer's disease. Pricing has yet to be determined.

Hemophilia

Private payers normally have nothing to do with drugs for hemophilia, which are blood products. However, the first oral therapy, fitusiran (brand name to be determined by manufacturer Sanofi), is on the horizon and may signify a shift in costs to private plans. The drug is in phase 3 clinical trials and has yet to be evaluated by any regulatory authority.

The FDA is reviewing Roctavian (valoctogene roxaparvovec), the first gene therapy for hemophilia. In August 2020, it announced it would delay its decision by a year or more, until it receives more clinical data from manufacturer BioMarin.

Dravet syndrome

One of the main ingredients in an old drug for weight loss—known as fen-phen and pulled off the market in the late 1990s for safety reasons—has found new purpose as a treatment for Dravet syndrome, a rare form of epilepsy. The FDA approved Fintepla (fenfluramine) in June 2020, though manufacturer Zogenix has yet to submit the drug to Health Canada for review. Based on its U.S. list price, the cost is about US$96,000 per year.

After the pipeline: Diabetes, migraine and multiple sclerosis.

Breakthrough therapies in the categories of diabetes, migraine and multiple sclerosis have set in motion a transformation of their respective markets. First, the new options represent major advances in treatment, particularly for those who struggle to manage their condition or who could not use previous therapies. As a result, patients who meet the treatment criteria appear to be steadily adding or switching to one of the new therapies.

Second, the new therapies' price points are significantly higher than those of older therapies, resulting in higher growth rates overall for eligible costs. While a positive return on investment is expected in terms of greater workplace productivity and reduced benefits costs in other areas, including disability, measures to monitor utilization and optimize outcomes are more important than ever.

Get the facts from 2021 Category Watch: The Impact of New Drugs, a report by TELUS Health.

Conclusion

Of the 10 new drug submissions reviewed in this report, just three can be described as "mainstream" in terms of potential patient populations: Reyvow for migraine, Leqvio for high cholesterol and Dayvigo for insomnia. A fourth, colchicine for COVID-19, may join that list, but its approval is uncertain and the patient population remains to be determined.

The remaining six drugs illustrate how medical research steadily advances treatment of much less prevalent conditions, such as multiple sclerosis and cystic fibrosis. While these diseases affect fewer people, they nonetheless represent significant cost burdens for the public healthcare system and employers (due to disability costs and lost productivity). However, the costs of these new treatments are high—in some cases, hundreds of thousands of dollars annually. A single claim could incapacitate a private drug plan. As a result, the next few years will likely see accelerated reforms—by public and private plans, and perhaps jointly—in the areas of market access, funding and plan design.

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