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The Drug Pipeline:

What's coming for private drug plans.

TELUS Health

Contents

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Introduction

More than 140 drugs are braced for launch from Canada's drug pipeline today, as they await regulatory approval from Health Canada. Cancer drugs are at the forefront, accounting for a third of all of these submissions. And more than half, including the cancer therapies, are higher-cost, specialty drugs, aimed at treating targeted patient populations—in some cases, for very rare diseases that up until now were considered virtually untreatable.

This article takes a closer look at 14 of these drugs, anticipated to have the most impact on private drug plans. All are specialty drugs—with cancer drugs dominating, as more of these medications become available in an oral pill format—and three of them are for relatively larger patient populations (to treat migraine, dry eye and severe asthma). The lowest anticipated cost among all of these drugs is about $6,400 per year (for migraine); the highest, for a very rare form of muscular dystrophy, is more than $700,000 per year.

We also take a look at what's happening among brand-name drugs that have reached patent expiry, and the resulting anticipated launches of generic and biosimilar drugs.

Drugs for cancer.

Vitrakvi, a breakthrough on several fronts.

Vitrakvi (generic name: larotrectinib) has captured headlines for a number of reasons since its approval by the U.S. Federal Drug Administration (FDA) in November 2018. First, as summarized in the FDA press release, it represents "a significant step in the development of cancer drugs that treat tumors based on the genetic properties of the tumor, rather than their location in the body." In other words, Vitrakvi can be used for any solid tumour that tests positive for certain genes, regardless of where the tumour is in the body. Traditionally, indications for cancer drugs are site-specific, for example, to treat breast cancer, colon cancer, etc.

Having said that, not many tumours will test positive for the genetic biomarkers. It's estimated that just 2,500 to 3,000 patients in the U.S. will develop cancers that meet the criteria for this drug. If we apply the traditional 10:1 ratio between populations in the U.S. and Canada, that translates into just 250 to 300 patients a year here.

The second reason why Vitrakvi is noteworthy, particularly for private drug plans, is the fact that it comes as a simple pill for adults, and an oral liquid for children. Therefore, private plans will likely be the first payer, rather than hospitals or public plans. In the U.S., Vitrakvi costs US$32,800 per month or about US$393,600 annually. The pediatric formulation costs about US$11,000 per month (US$132,000 annually). Patients may take the drug for weeks or years, depending on disease progression.

Last but not least, the drug is making headlines because its manufacturer, Bayer, has promised affordability for patients and a value-based reimbursement model for payers. The company has stated that the average monthly out-of-pocket cost for most patients will be $20 or less, and has established a charity to this end. And Bayer will refund payments to private and public payers if the drug does not show clinical benefit during the first three months of treatment.

Health Canada accepted Bayer's submission of Vitrakvi for review in November 2018, and we can probably expect approval by the end of this year.

Idhifa for leukemia.

When Idhifa (enasidnib mesylate) was approved by the FDA in August 2017, it was the first oral drug to treat a certain genetic mutation of acute myloid leukemia. It will soon be available in Canada as well, following Health Canada's approval in February 2019.

The estimated patient population in the U.S. is just 1,200 to 1,500 adults, which would be less than 200 in Canada. While pricing details for Canada are still to come, the cost in th U.S. is about US$24,900 per month, or US$300,000 per year.

Lorbrena for lung cancer.

Lorbrena (lorlatinib) joins a number of other drugs used to treat an aggressive form of non-small cell lung cancer that tests positive for a certain gene mutation. It is not, however, a "me-too" drug. It can be an additional, vital line of therapy for patients, many of whom experience a worsening of the disease despite initial positive responses to previous drugs.

The manufacturer, Pfizer, submitted Lorbrena for Health Canada review in June 2018, and approval is expected by mid-2019. The FDA approved it in November 2018. The cost in the U.S. is about US$16,800 per month, or US$201,300 annually.

Epidemiology studies suggest that three to five per cent of non-small lung cancers test positive for the gene mutation that can be treated by this class of drugs. This represents a patient population of 6,000 to 10,000 in the U.S., or 600 to 1,000 in Canada.

Nerlynx for early breast cancer.

When approved in the U.S. in July 2017, Nerlynx (neratinib) was the first adjuvant therapy for early-stage HER2-positive breast cancer, which tends to be more aggressive than HER2-negative breast cancer. As an adjuvant drug, Nerlynx is taken along with the traditional initial line of therapy, to further reduce the risk of the cancer recurring. The cost is about $149,300 for the recommended one year of treatment ($11,700 per month).

Approximately 20 per cent of breast cancer patients are HER2-positive. In Canada, this represents a patient population of 5,000 to 5,500.

The European Commission approved Nerlynx in September 2018, despite initial concerns from the European Medicines Agency regarding efficacy and safety. The Agency had advised against approval until the manufacturer, Puma Biotechnology, submitted new data that better demonstrated the drug's efficacy.

Puma submitted Nerlynx for review by Health Canada in September 2018.

Talzenna for advanced breast cancer.

Talzenna (talazoparib) is indicated for HER2-negative, advanced breast cancer (i.e., that has spread) with certain genetic mutations. The FDA approved Talzenna in October 2018, and Health Canada began its review in November 2018.

The cost is about US$15,300 per month, or $184,200 per year.

Zejula for ovarian and other cancers.

Zejula (niraparib) is a maintenance, oral drug for women with certain types of ovarian, fallopian tube or primary peritoneal cancer. Pricing can range from US$9,800 per month (US$117,600 per year) to US$14,800 per month ($177,600 per year), depending on patients' dosing requirements. Health Canada began its review in September 2018.

At the time of its approval in the U.S. in March 2017, Zejula was the first drug indicated for use after the cancer comes back following chemotherapy. Since then, however, Lynparza (olparib) has also become available, approved by Health Canada in May 2018 and by the FDA in December 2018. The cost of Lynparza in Canada is approximately $7,500 per month.

Keytruda for additional cancer indications.

Keytruda (pembrolizumab), an immunotherapy treatment administered by infusion, is already approved in Canada for specific indications linked to non-small cell lung cancer, Hodgkin lymphoma, melanoma and urothelial cancer. For example, in the case of non-small cell lung cancer, it is used as a first line of therapy based on a certain genetic biomarker, when the cancer has spread to other parts of the body, and the patient has not had chemotherapy.

Keytruda's manufacturer, Merck Canada, is now seeking approval from Health Canada for six additional, specific indications. In the U.S., the FDA has approved Keytruda for a total of 17 indications since initial approval in 2014. Six of the FDA approvals occurred in 2018 and the most recent one, authorizing Keytruda's use as an adjuvant treatment for melanoma patients with lymph node involvement, occurred in February 2019.

The cost, which has been fairly consistent across all indications so far, is about $11,700 for four weeks, or about $152,000 per year.

Drugs for larger patient populations.

More biologics for migraine.

Emgality (galcanezumab-gnim) will be the second biologic in Canada for the prevention of migraine in adults, if approved by Health Canada. The first, Aimovig (erenumab), became available in December 2018, at a cost of about $6,400 per year.

Manufacturer Eli Lilly submitted Emgality to Health Canada in October 2018, which means the drug will likely be approved, and launched, this fall. The FDA approved the drug in September 2018. Its cost in the U.S. is US$575 per month, or US$6,900 per year. Both drugs are self-injected once a month.

While as many as three million Canadians suffer from migraine, these biologic drugs are indicated only for those who have at least four migraine days per month. This results in a patient population of about 700,000 in Canada. We can expect to see more entries in this new category of biologics in the coming years.

Cequa for dry eye.

The prevalence of dry eye increases with age, and can be as high as 30 per cent in persons aged 50 and older, depending on the country. In the U.S. it affects approximately seven per cent of the population overall, which would translate into about 2.5 million Canadians.

In December 2018, Health Canada approved Cequa (cyclosporin), eye drops that are the first to incorporate nanomicellar technology for improved penetration into the eye. Private drug plans will likely put prior authorization in place to ensure Cequa is not the first line of therapy for patients, given its price tag. While the manufacturer, Sun Ophthalmics, has yet to release pricing information for Canada, south of the border Cequa retails for about US$550 per month (US$6,600 per year).

Dupixent for severe asthma.

Approximately 250,000 Canadians have severe asthma, which can be life-threatening. Dupixent (dupilumab), a biologic already available in Canada for moderate to severe eczema, is now seeking approval as a treatment for severe asthma. FDA approved it as an asthma treatment in October 2018, where it costs about US$37,000 per year.

Dupixent will enter an already crowded space, as several other biologic drugs to treat severe asthma have been available for at least two years in Canada. Their list prices are in the range of $30,000 per year, though it can be less depending on dosing requirements. Health Canada began its review in November 2018.

High-cost orphan drugs for rare conditions.

Ultomiris for blood disorder, a replacement for Soliris.

Paroxysmal nocturnal hemoglobinuria (PNH) is an extremely rare, life-threatening blood disease that affects one to 10 people per million. Ultomiris (ravulizumab), approved by the FDA in December 2018 after an expedited review period, is the first long-acting treatment for the condition. The estimated annual cost of this biologic drug is US$458,000.

Ultomiris is intended to replace Soliris (eculizumab) as a treatment for PNH. Both are produced by Alexion Pharmaceuticals. Ultomiris is more convenient, since it is administered by infusion every eight weeks rather than every two weeks, as required for Soliris. The manufacturer has also estimated that the price of Ultomiris will be 10 per cent lower than Soliris, on average.

Health Canada initiated its review of Ultomiris in November 2018, with approval expected before the end of this year.

Translarna for muscular dystrophy.

Translarna (ataluren) is a breakthrough drug for Duchenne muscular dystrophy, a rare neuromuscular disease with an estimated patient population of just 800 in Canada. The majority of patients are young boys.

The European Medicines Agency granted conditional approval—meaning it has requested ongoing additional clinical data from the manufacturer, to confirm the drug's efficacy and safety—in 2014. The FDA declined approval of Translarna in September 2017, citing the need for more research. However, it remains available in the U.S. through clinical trials. Health Canada began its review in September 2018.

In Europe, the cost of Translarna is about €411,000 annually, which would be about $704,000 in Canadian dollars. The drug, an oral liquid, can be self-administered.

Alofisel for Crohn's disease.

Alofisel (darvadstrocel) is a breakthrough therapy in that it uses human stem cells to treat a complication of Crohn's disease. It is indicated for use after the patient has had an inadequate response to at least one biologic medication. A clinical review published in the December 2018 edition of BioDrugs describes it as "a promising, novel, minimally invasive therapy that represents an important advance in… therapeutic options."

The drug was approved in Europe in May 2018. It remains under review in the U.S., and Health Canada began its review in August 2018.

The drug, which must be injected by a healthcare professional, costs €54,000 for a once-a-year treatment in Europe, or approximately $93,300 in Canadian dollars.

Oxervate for rare eye disease.

Oxervate (cenegermin) is for neurotrophic keratitis, a rare degenerative disease of the eye that affects less than five in 10,000 people. The drug received approval in Europe in July 2017, in the U.S. in August 2018, and was just approved by Health Canada in February 2019.

In the U.S., the cost for the eight-week treatment is about U$50,000 to US$55,000.

Table 1

Drug name	Disease/ indication	Drug format	Anticipated timing	Estimated cost*
Vitrakvi	Non-site-specific cancer tumours	Oral pill	Health Canada review initiated in November 2018; approval likely in late 2019.	Up to $520,000 annually
Idhifa	Acute myloid leukemia	Oral pill	Review launched in July 2018; approval anticipated by mid 2019.	$396,500 annually
Lorbrena	Non-small cell lung cancer	Oral pill	Review initiated in June 2018; approval expected by mid 2019.	Up to $266,000 annually
Nerlynx	Breast cancer	Oral pill	Review initiated in September 2018; approval likely by end of 2019.	$197,000 for recommended one year of treatment
Talzenna	Breast cancer	Oral pill	Review begun in September 2018; approval anticipated by end of 2019.	Up to $243,400 annually
Zejula	Ovarian and other cancers	Oral pill	Review initiated in September 2018; approval expected by end of 2019.	From $155,400 to up to $234,700 annually
Keytruda	Melanoma and other cancers	Infusion	Reviews for up to six new indications launched from September 2017 to October 2018; approvals expected throughout 2019 and possibly into 2020.	Up to $152,000 annually
Egality	Migraine	Self-injection	Review initiated in October 2018; approval expected by end of 2019.	$6,400 annually
Cequa	Dry eye	Eye drops	Approved by Health Canada in December 2018; market launch imminent.	$8,700 annually
Dupixent	Severe asthma	Self-injection	Review initiated in November 2018; approval expected by end of 2019.	Up to $48,900 annually
Ultomiris	Rare blood disorder	Infusion	Review begun in November 2018; approval expected by end of 2019.	$605,000 annually
Translarna	Duchenne muscular dystrophy	Oral liquid	Review started in September 2018; approval expected by end of 2019.	$704,000 annually
Alofisel	Crohn's disease	Injection by health professional	Review initiated in August 2018; approval anticipated by mid-2019.	$93,300 for once-a-year treatment
Oxervate	Rare eye disease	Eye drops	Review started in August 2018; approval expected by mid-2019.	$66,000 to $73,000 for one-time treatment

*Based on pricing information in the U.S. or Europe, converted to Canadian dollars.

Biosimilars

When it comes to biosimilar biologics likely to be covered by private drug plans, no launches are expected in 2019. A possible exception could come in the form of up to four biosimilars for Rituxan (rituximab), used to treat non-Hodgkin's lymphoma as well as rheumatoid arthritis. These have been under Health Canada review for just over a year; however, the submissions from the manufacturers appear to be limited to the cancer indication, which would not affect private plans. If Health Canada extrapolates its reviews to include the indication for rheumatoid arthritis, which is possible, then the door opens to coverage by private plans.

As well, in May 2018 Health Canada approved the first biosimilar for Humira (adalimumab), used for rheumatoid arthritis and other autoimmune conditions, and approvals for two more adalimumab biosimilars are expected this year. However, a litigation settlement will likely keep these biosimilars off the market until 2021. Two additional adalimumab biosimilars may also be submitted in the near future, following recent regulatory approvals in Europe and the U.S.

Table 2 summarizes the biosimilars that are currently pertinent for private drug plans.

Table 2

Biosimilar name (manufacturer)	Brand name (reference drug)	Disease/indication	Anticipated timing	Estimated cost of biosimilar*
Hadlima (Merck)	Humira (adalimumab)	Rheumatoid arthritis and other autoimmune conditions	Approved by Health Canada in May 2018; however, litigation will likely delay launch until 2021.	$27,000 - $31,000 per year, based on dosage requirements
Amjevita (Amgen)	Humira (adalimumab)	Rheumatoid arthritis and other autoimmune conditions	Health Canada approval expected in 2019; however, litigation will likely delay launch until 2021.	$27,000 - $31,000 per year, based on dosage requirements.
Hyrimoz (Sandoz)	Humira (adalimumab)	Rheumatoid arthritis and other autoimmune conditions	Health Canada approval expected in 2019; however, litigation will likely delay launch until 2021.	$27,000 - $31,000 per year, based on dosage requirements.
Hulio (Mylan)	Humira (adalimumab)	Rheumatoid arthritis and other autoimmune conditions	Not yet submitted to Health Canada.	$27,000 - $31,000 per year, based on dosage requirements
Imraldi (Biogen)	Humira (adalimumab)	Rheumatoid arthritis and other autoimmune conditions	Not yet submitted to Health Canada.	$27,000 - $31,000 per year, based on dosage requirements

*Based on list price that is 20% to 30% lower than originator biologic's list price, according to Pharmacoeconomic Review Report by the Common Drug Review, CADTH.

Generics

This year may see zero market launches for generic drugs in Canada, due to ongoing patent litigation. Generic versions of Pradaxa, an anticoagulant, may be the only exceptions, though it's difficult to predict when litigation will be resolved. Table 3 summarizes what we can expect in the near future.

Table 3

Drug name	Disease/indication	Notes
Pradaxa	Anticoagulant (blood thinner) to reduce risk of strokes and blood clots	Generics for Pradaxa were approved by Health Canada in February 2018, but marketing has been delayed by litigation.
Gilenya	Relapsing-remitting multiple sclerosis	Patent expiry in March 2019.
Advagraf	Immunosuppressant following organ transplant; can also be used for rheumatoid arthritis	Patent expiry March 2019; anticipated regulatory approval and launch of at least one generic in 2019.
Zytiga	Prostate cancer	Patent expiry in July 2019; pending litigation, however, could delay generic entry until 2027.
Imraldi (Biogen)	Humira (adalimumab)	Rheumatoid arthritis and other autoimmune conditions

Conclusion

Without doubt, Canada's drug pipeline represents a growing dichotomy between unprecedented innovation for patients, and challenges in affordability for payers. In the private sector, regulatory approval is no longer necessarily synonymous with coverage, as many benefits providers conduct an additional layer of review, and put in place prior authorization and other mechanisms to ensure appropriate access and optimal use.

We can expect continued evolution in market access and drug plan design in the coming years, including the emergence of value-based reimbursement models, as pharmaceutical manufacturers, payers and patient groups strive to balance health with sustainability.

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