Drug pipeline, what lies ahead for private plans

Considerations for employer benefit plans

ALBERTA BLUE CROSS®

CONTENTS

EXECUTIVE SUMMARY

Every year, advancements and innovations in drug therapies provide important, life-changing treatments for plan members. However, with many new therapies being higher in cost, significant pressure has been placed on the sustainability of private drugs plans. This report highlights some new and notable developments in the drug pipeline to provide insight into what may lie ahead for your benefit plan and your employees.

DRUG PIPELINE AT A GLANCE

- With the introduction of new medications for more common health conditions, such as migraine, asthma and depression, the number of high-cost, specialty and biologic medications entering the market is increasing. The potential annual costs of the drugs noted in this document range from $6,400 to over $100,000 CAD. Having high-cost drugs for more prevalent conditions will create increased utilization and along with it, increased drug spend.
- The approval of first-entry generic drugs and biosimilars offers savings compared to the brand name and innovator biologic counterparts. Generics are coming for oral multiple sclerosis therapies, some blood thinners and a commonly used diabetes medication. Several new biosimilars have been approved, but market launch may be delayed for some.
- Drugs for rare conditions are some of the highest cost drugs available, and new breakthrough medications are continually emerging. Though these conditions afflict a small portion of the population and the drugs used to treat them may fall under alternate funding sources provided by the government, they have the potential to significantly impact private plans.
- Gene therapy is an innovative advancement in drug treatment that is being used to treat or even cure previously intractable diseases. These groundbreaking therapies are accompanied by high price tags ranging from $65,000 to over $2 million USD and are presently most commonly used for cancer. However, their use in more common conditions, such as cardiovascular disease or Alzheimer's disease, is currently under development.

BACKGROUND

There are currently over 200 drug submissions with Health Canada that are under review as a new drug product, a generic or biosimilar drug or for a new indication on an existing drug therapy. With the vast number of drugs under review, this document highlights those therapies that carry the greatest potential of impacting private drug benefit plans.

When a medication is submitted to Health Canada for approval, it takes close to one year before a decision is rendered to either approve the therapy by providing a Notice of Compliance (NOC), or deny the application with a Notice of Noncompliance (NON). This process is condensed to approximately 215 days when a drug receives priority review status. Given the duration of Health Canada's approval process, we focused our review on drugs already submitted to Health Canada as this will capture most drugs likely to be launched in the Canadian market within the next year. We have also included some information on significant drugs that have just received Health Canada approval or where market launch has occurred within the past few months. Not included is a review of medications for cancer or HIV, as there are government programs that may provide funding for medications with these indications.

Since drugs are often approved in other countries before they are approved in Canada, we have included pricing from these other jurisdictions. However, it should be noted that this pricing is intended as a reference point only as Canadian pricing may be different and won't be available until the drug is on the Canadian market. Drug pricing in Canada is also subject to approval by the Patented Medicine Prices Review Board (PMPRB).

In addition to new drug therapies, the approval of first-entry generics and biosimilar medications can influence drug spend on a benefit plan as these therapies are priced lower. As such, we will outline first-entry generic and biosimilar drugs that have recently entered the Canadian market, or may soon be entering the market based on submissions under review, recent approvals by Health Canada and data protection expiries.

Finally, with the growing interest in emerging gene therapies, we will briefly explore the status of these breakthrough therapies.

NOTABLE HIGH-COST DRUGS

High-cost and specialty medications were historically used for conditions that afflicted a small portion of the population, whereas now we are seeing an increasing number of high cost drugs entering the market for more common health conditions such as migraine, asthma and depression. Having specialty drugs for such indications will create increased utilization, which can vastly impact drug spend.

SPRAVATO

Spravato (esketamine) nasal spray, with the first new mechanism of action for treating depression seen in decades, was approved in the US in March 2019 and is currently under priority review with Health Canada. Spravato is a breakthrough therapy for treatment resistant depression, which affects almost a quarter of those with major depressive disorder. Manufacturer trials have shown significant improvement in patients who suffer from this condition, but due to the active ingredient being related to ketamine, a potent anesthetic and known street drug, there is potential for serious risks and adverse reactions. The Food and Drug Administration (FDA) will be launching Spravato in the US under a Risk Evaluation and Mitigation Strategy (REMS), ensuring Spravato is only dispensed and administered under direct supervision of a certified health care professional and the patient is monitored for two hours post-administration. Spravato will be an add-on to oral antidepressants and its US cost is up to $45,000 USD annually.

EMGALITY AND AJOVY

Calcitonin Gene-Related Peptide (CGRP) inhibitors, a new class of biologic drugs, have recently emerged for prevention of migraine in adults. Migraine is a chronic, neurologic disorder that afflicts approximately 8.3 per cent of Canadians, likely with an additional cohort of undiagnosed sufferers. Manufacturer studies show that this new class of treatments can reduce migraine days, presenteeism, absenteeism and costs for acute migraine drugs. Emgality is the second CGRP inhibitor to become available in Canada, subsequent to Aimovig, and is currently available at a list price of $7,500 CAD annually. A third option may soon become available for Canadians suffering from migraine, as Ajovy is currently under review with Health Canada. While all three CGRP inhibitors use a monthly dosing regimen, Ajovy also offers an alternative four times a year dosing option with administration every three months. The current list price for Ajovy in the US is $6,900 USD annually.

MAYZENT

Mayzent (siponimod) was recently approved in the US in March 2019 for relapsing forms of Multiple Sclerosis (MS), including Clinically Isolated Syndrome (CIS), Relapsing-Remitting MS (RRMS) and Secondary Progressive MS (SPMS), and is currently under review in Canada. It is the inclusion of SPMS in its indication that makes this drug unique from other oral medications currently available. Most people who are diagnosed with RRMS will go on to develop SPMS, a debilitating form of MS that involves progressive worsening of neurological function. Manufacturer studies have shown Mayzent reduces the risk of disease progression, physical disability, and cognitive decline. The current list price in the US for Mayzent is $88,500 USD annually.

OVERVIEW

DRUG	MANUFACTURER	INDICATION	HEALTH CANADA STATUS	PRICING IN OTHER COUNTRIES*
Spravato (esketamine)	Janssen	Nasal spray for treatment resistant major depressive disorder	Under priority review since January 2019	$38,000 to $60,000 per year [i]
Emgality (galcanezumab)	Eli Lilly	Prevention of migraine in adults	Marketed October 2019	$7,500 per year †
Ajovy (fremanezumab)	Teva	Prevention of migraine in adults	Under review since June 2019	$9,200 per year [ii]
Mayzent (siponimod)	Novartis	Secondary progressive multiple sclerosis (SPMS)	Under review since February 2019	> $110,000 per year [iii]

**Converted to Canadian dollars*
†Canadian list price

FIRST-ENTRY GENERIC DRUGS

When a new brand name drug is developed by a manufacturer, it holds patent and data protection for a pre-defined time period. Once patent and data protection ends (via expiry or litigation), the generic formulations can enter the Canadian market.

PRADAXA AND ULORIC

Apotex's generic drug for Pradaxa, a medication for thinning the blood, became available in February 2019 for two of the three available strengths; launch to the rest of Canada and the remaining strength occurred shortly thereafter. In April 2019, Teva and Marcan received approval for their generic formulations of Uloric, a medication used to reduce uric acid levels in patients with gout, but only Marcan's product is currently marketed. The generic drugs for Pradaxa and Uloric offer savings of approximately 25 per cent compared to the brand name drugs.

GILENYA, FAMPYRA AND TECFIDERA

Until recently, there were no generic alternatives available for oral drugs indicated for MS and annual treatment costs with these therapies can reach up to $31,000 CAD. Multiple generic formulations for Gilenya have become available in the last few months and are currently listed from 25 to 85 per cent of the brand name cost. Additionally, Fampyra and Tecfidera currently have generic submissions under review.

JANUVIA, ELIQUIS, AND XARELTO

First-entry generics that are currently under review with Health Canada include Januvia, used to reduce blood glucose levels in those with type 2 diabetes mellitus, and Eliquis and Xarelto, therapies for thinning the blood. The dates of these generic submissions are not listed by Health Canada, making it difficult to predict when approval and market entry may occur.

OVERVIEW

BRAND NAME	THERAPEUTIC USE	GENERICS UNDER HEALTH CANADA REVIEW	GENERICS APPROVED	GENERIC(S) MARKETED
Pradaxa (dabigatran)	Blood thinner		✓	✓
Uloric (febuxostat)	Gout		✓	✓
Gilenya (fingolimod)	Multiple sclerosis		✓	✓
Fampyra (fampridine)	Multiple sclerosis	✓		
Tecfidera (dimethyl fumarate)	Multiple sclerosis	✓		
Januvia (sitagliptin)	Type 2 diabetes mellitus	✓		
Eliquis (apixaban)	Blood thinner	✓		
Xarelto (rivaroxaban)	Blood thinner	✓		

BIOSIMILARS

Biosimilars, biologic drugs that have entered the market subsequent to an innovator biologic, can provide cost savings over innovator biologic medications. According to the Canadian Agency for Drugs and Technologies in Health (CADTH), new biosimilars in Canada are usually priced at 12-23 per cent less than their reference product. Unlike generic medications, biosimilars are not interchangeable with the innovator due to the complexity of the molecules involved. This means that members would require a new prescription when switching from an innovator to a biosimilar.

HUMIRA, NEULASTA, NEUPOGEN AND RITUXAN BIOSIMILARS

Hadlima, the biosimilar for Humira, has been much anticipated by clinicians and patients since its approval in May 2018. However, market launch is not expected until 2021 due to a litigation settlement. Hadlima will cover the same array of autoimmune disorders as Humira, including such conditions as rheumatoid arthritis, plaque psoriasis and ulcerative colitis, providing a large market for utilization upon its availability.

Neulasta and Neupogen are used to prevent infection in patients on antineoplastic medications. Neulasta already has a biosimilar marketed in Canada, Lepalga, and will soon have a second biosimilar to compete with as Fulphila received approval in December 2018 and is now awaiting market launch. Neupogen has two biosimilars currently under review with Health Canada and they will join the already marketed biosimilar, Grastofil, upon their approval.

Rituxan's first biosimilar, Truxima, which has already launched in 26 European countries, received Health Canada approval in April 2019 for treatment of rheumatoid arthritis as well as some cancer indications. There are several additional biosimilar drugs currently under review with Health Canada, indicating the biosimilar environment in Canada will continue to grow as more of these therapies become available.

OVERVIEW

INNOVATOR BIOLOGIC	BIOSIMILAR	MANUFACTURER(S)	INDICATION(S)	HEALTH CANADA STATUS
Humira	Hadlima*	Samsung Bioepis Co.	Numerous autoimmune disorders including Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA), Crohn's Disease (CD), and Ulcerative Colitis (UC)	Approved in May 2018, market entry not expected until 2021
Neulasta	Fulphila*	BGP Pharma (Mylan)	Reduce incidence of infection (febrile neutropenia) in patients receiving anti-neoplastic drugs	Approved in December 2018, market entry unknown
Neupogen	To be confirmed	Pfizer and Tanvex Biopharm	Reduce incidence of infection (febrile neutropenia) in patients receiving anti-neoplastic drugs	Two submissions currently under review
Rituxan	Truxima*	Celltrion Healthcare Co.	Rheumatoid arthritis and some cancer indications	Approved in April 2019, market entry unknown

**There are several additional biosimilar submissions currently under review by Health Canada for the innovator biologic.*

DRUGS FOR RARE CONDITIONS

Drugs for the treatment of rare conditions are important life-changing therapies for those afflicted, but are also among the highest costing medications on the market. Most of these medications treat diseases that previously had no or limited drug treatments. We watch these drugs closely for alternate funding or inclusion in government programs to protect plan sponsors should a member require one of these high-cost therapies.

ULTOMIRIS

Ultomiris (ravulizumab) is a biologic medication for treatment of a rare and potentially life-threatening blood disease known as paroxysmal nocturnal hemoglobinuria (PNH). This disease affects only approximately 90 people in Canada. Made by the same manufacturer as Soliris, Ultomiris is meant to replace Soliris as it has a more attractive dosing regimen of administration every eight weeks versus every two weeks. Health Canada approved Ultomiris in August 2019; however, the date of expected market launch and the Canadian list price is not yet known. The estimated annual cost of Ultomiris in the US is more than $450,000 USD for an average weight adult.

CABLIVI

Cablivi (caplacizumab) offers a much needed treatment option for patients afflicted with a rare, life-threatening blood disorder known as acquired Thrombotic Thrombocytopenic Purpura (aTTP). Despite current standard of care with urgent treatment of plasma exchange and immunosuppression, an estimated 20% of patients die from aTTP episodes. Cablivi is approved in the US and Europe as an add-on treatment option and has a US cost of $270,000 USD for treating a typical aTTP episode. Cablivi was submitted to Health Canada for review in August 2019.

OVERVIEW

DRUG	MANUFACTURER	INDICATION	HEALTH CANADA STATUS	PRICING IN OTHER COUNTRIES*
Ultomiris (ravulizumab)	Alexion Pharmaceuticals	Paroxysmal nocturnal hemoglobinuria (PNH)	Approved August 2019, market entry unknown	>$600,000 per year [iv]
Cablivi (caplacizumab)	Sanofi	Acquired thrombotic thrombocytopenic purpura (aTTP)	Under review since August 2019	>$350,000 per treatment course [v]

**Converted to Canadian dollars*

GENE THERAPY

Gene therapy is a promising and innovative advancement in drug treatment, with multiple mechanisms being actively researched and in various stages of development. Gene therapy involves the introduction of genetic material into a patient, either by injecting gene therapy directly into the body or by extracting a patient's own cells to make modifications and then re-infuse into the body. Unlike current drug therapies, gene therapy uses techniques to alter a person's genes to treat or cure diseases. Therefore, the patient usually only requires a single treatment. The customization and complexity of these therapies, as well as their ability to offer a potential cure for previously intractable diseases, leads to a high price point; currently available global pricing shows costs that range from $65,000 to over $2 million USD.

The two gene therapies that have been approved in Canada, Kymriah and Yescarta, have not had their costs disclosed publicly and are currently indicated for certain forms of cancer. Kymriah recently became available in Quebec in October 2019 and will fall under government funding at this time. While these therapies may be government funded due to their cancer indications, it is important to note that there is ongoing interest and research in developing gene therapies for treatment of more common disorders such as cardiovascular disease and degenerative disorders of the nervous system like Parkinson's disease and Alzheimer's disease.

Many factors that will need to be considered by government, manufacturers, and insurers before gene therapy can be widely utilized, such as the complexity of administration, the requirement of specialized clinicians; clinics and monitoring; and high associated costs. We will be closely observing the development of these breakthrough therapies so that we can keep plan sponsors current and prepared for any potential future implications.

ALBERTA BLUE CROSS DRUG MANAGEMENT STRATEGY

Alberta Blue Cross has numerous controls and optional plan management features that mitigate rising drug costs and ensure plan sustainability.

- Comprehensive drug review process—when new medications enter the Canadian market, they are thoroughly reviewed by our in-house pharmacists and Drug Review Committee who critically assess the scientific, therapeutic and economic value of each drug before a listing decision is rendered.
- Managed formulary—plan sponsors can choose to adopt this formulary, which includes a number of management features, such as special authorization, that protects plan sponsors as the market for high-cost therapies continues to expand.
- Special authorization—a standard feature on our managed formulary and is applied to high-cost drugs where there is opportunity to ensure those therapies are covered only for members meeting clinical criteria. Additionally, special authorization ensures members are accessing any publicly funded drug programs first before coverage is granted on their private plan.
- Drug price management—Alberta Blue Cross has extensive management of drug prices to ensure we provide the best value for your plan. We have a dedicated team who is responsible for maintaining our drug price files; we continually review the prices that manufacturers and wholesalers are charging for their drugs to ensure our files reflect the current drug price landscape.
- Responsive management strategies—We continue to monitor the drug environment as utilization and government policies evolve and will continue to adapt our listing strategies to ensure continued optimal management and savings for our drug plans.

COST LISTING REFERENCES:

(i) https://www.fiercepharma.com/pharma/icer-takes-issue-johnson-johnson-s-spravato-price-questions-breadth-data

(ii) https://www.marketwatch.com/press-release/teva-announces-us-approval-of-ajovytm-fremanezumab-vfrm-injection-the-first-and-only-anti-cgrp-treatment-with-both-quarterly-and-monthly-dosing-for-the-preventive-treatment-of-migraine-in-adults-2018-09-14

(iii) https://www.biopharmadive.com/news/novartis-mayzent-multiple-sclerosis-approval-secondary-progressive/551419/

(iv) https://www.investors.com/news/technology/alexion-blood-disease-drug-ultomiris/

(v) http://www.news.sanofi.us/2019-02-06-FDA-approves-Cablivi-R-caplacizumab-yhdp-the-first-Nanobody-R-based-medicine-for-adults-with-acquired-thrombotic-thrombocytopenic-purpura-aTTP

QUESTIONS?

If you'd like to learn more, please contact us at **1-866-513-2555**.