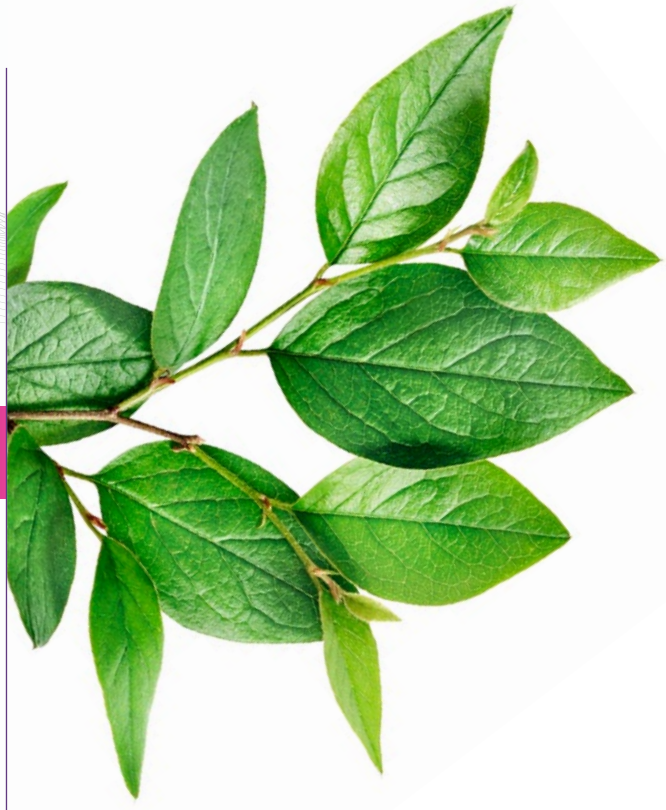
Perspectives | Spring 2022



The Drug Pipeline: What private plans can expect in 2022.

TELUS Health

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Introduction

As of February 16, 2022, Health Canada was reviewing 142 drug submissions, down slightly from more than 150 at this time last year. Similar to last year, just over half (75) are for new drugs, with the remainder (67) being for new indications for drugs already on the market.

TELUS Health has identified potentially costly new drugs for several conditions that affect large numbers of Canadians, including Alzheimer's disease, macular degeneration and atopic dermatitis (also known as eczema). We've also highlighted the approval of new generics to treat multiple sclerosis, a rare condition but among the top 10 contributors to plan costs.

Finally, we've discussed new treatments for COVID-19 that can be administered outside hospitals—although it is expected these will be publicly funded for the time being.

What to expect for:

Alzheimer's disease

The Alzheimer Society of Canada reports that more than 500,000 Canadians currently have dementia, and that number is expected to rise to 912,000 by 2030.[1] Alzheimer's disease is the most common form of dementia.

Three cholinesterase inhibitors are approved for mild and moderate dementia: donepezil, rivastigmine and galantamine. One other drug, memantine, is an n-methyl-D-aspartate receptor antagonist approved for moderate to severe dementia.[2] All are designed to improve cognition, but do not address the underlying biology of Alzheimer's.

Biogen is aiming to change that with Aduhelm (aducanumab), a monoclonal antibody that aims to clear amyloid plaques in the brain. It was approved by the U.S. Food & Drug Administration (FDA) in June 2021 and submitted to Health Canada that same month. The FDA decision was not without controversy, because Biogen ended both of the drug's phase 3 trials in March 2019 due to "futility," and 10 out of 11 members of the FDA's independent expert advisory committee voted against its approval (with one "uncertain" vote) in November 2020. However, the drug was approved based on a subset of patients in one of the trials.

That said, FDA approval of Aduhelm raises the possibility of future approvals for drugs with similar mechanisms from both Eli Lilly (donanemab) and Roche (gantenerumab). Furthermore, while the FDA recommended that Aduhelm be limited to those with mild symptoms (the population studied in the clinical trials), U.S. physicians can choose to prescribe it to the wider population of people with moderate to severe symptoms.

Meanwhile, Biogen has funded an online symptom screener that suggests people who sometimes forget appointments or lose the thread of a conversation should talk to their doctor and seek additional testing. If Aduhelm is approved in Canada, this type of marketing could broaden the drug's reach to more of the working-age population. In Canada, close to 800,000 people have mild cognitive impairment.[3]

While we do not know Canadian pricing at this time, the U.S. cost is well documented. With intravenous infusions required every four weeks, and each infusion costing US$4,312, benefits plans may face per-patient costs for Aduhelm of US$56,000 a year.[4] It's worth noting that several large commercial insurers in the U.S. have already stated they will not cover Aduhelm.[5]

[1] https://alzheimer.ca/en/about-dementia/what-dementia/dementia-numbers-canada
[2] https://www.cihi.ca/en/dementia-in-canada/spotlight-on-dementia-issues/dementia-prevention-and-treatment
[3] https://www.cmaj.ca/content/193/36/E1430
[4] https://www.cnn.com/2021/06/09/health/aducanumab-questions-answered-wellness/index.html
[5] https://journals.lww.com/neurotodayonline/fulltext/2021/09160/new_questions_raised_about_costs,_coverage_for.5.aspx

Macular degeneration

Almost two million Canadians have age-related macular degeneration (AMD), and the Canadian Ophthalmological Society estimates that AMD is responsible for 90 per cent of new cases of legal blindness.[6] There is no treatment for "dry" AMD, but injections can help slow the progression of "wet" AMD.

Two of the market-leading wet AMD drugs in Canada are Novartis's Lucentis (ranibizumab) and Bayer and Regeneron's Eylea (aflibercept). Each Lucentis injection costs about $1,800 in Canada and the average patient needs six treatments annually.[7] Eylea is priced slightly lower per injection and may require fewer treatments annually.[8] Nonetheless, both are costly for insurance plans, so it's welcome news that several biosimilars are in development as Lucentis and Eylea near the end of their patent life cycle. A biosimilar for Lucentis arrived in 2022, with biosimilars for Eylea likely to follow around 2024.

In March 2022, Health Canada approved Byooviz, a Lucentis biosimilar developed by Samsung Bioepis and Biogen. Approved by the FDA in September 2021, it is expected to launch in the United States this summer.

As part of a two-pronged approach to treating wet AMD, Hoffmann-La Roche submitted a new medication designed to treat wet AMD and diabetic macular edema to Health Canada in 2021. Phase 3 studies showed that faricimab could double the time between treatments compared to aflibercept, providing equivalent vision gains with injections occurring at intervals of up to four months.[9] Hoffmann-La Roche has also submitted Susvimo (ranibizumab) implants, which were approved in the United States in October 2021. This new, longer-lasting form of ranibizumab may slow the uptake of biosimilar ranibizumab if Lucentis patients are migrated to this new delivery system.

Another effort to provide durable efficacy in the treatment of wet AMD is Kodiak's KSI-301, which may also lengthen treatment intervals and allow patients with intraocular inflammation to access treatment. Topline data from the phase 2b/3 study, which will compare it directly to Eylea and Novartis's Beovu (brolucizumab), is expected to be released in the first quarter of 2022. While Kodiak doesn't have a strong presence in Canada, this molecule is worth watching in the future.

Atopic dermatitis

Atopic dermatitis (AD) will affect about 17 per cent of Canadians at some time during their lives, according to the Canadian Dermatology Association,[10] and Atopic Dermatitis in America estimates that 40 per cent of people with AD experience moderate to severe symptoms.[11]

Treatment options include several high-cost drugs, such as Dupixent (dupilumab) and the more recently approved Adtralza (tralokinumab) and Rinvoq (upadacitinib). In its reviews recommending that public payers should not reimburse these medications, the Canadian Agency for Drugs and Technologies in Health (CADTH) estimated annual costs at more than $30,000 (after $31,154 in the first year) for Dupixent[12] and $21,633 (after $22,802 in the first year) for Adtralza.[13] CADTH recommended orally delivered Rinvoq for reimbursement for the treatment of rheumatoid arthritis at an estimated annual cost of $17,770.[14]

Health Canada is in the process of reviewing Pfizer's orally delivered Cibinqo (abrocitinib), approved in January 2022 by the FDA. One significant factor that may affect uptake for both Rinvoq and Cibinqo is that they are Janus kinase (JAK) inhibitors, a drug class that the FDA has flagged for serious adverse events.[15] The FDA requires both of these drugs to include warnings related to an increased risk of heart attack, stroke, cancer, blood clots and death. For its part, Health Canada approved Rinvoq with a restrictive indication that positions it as a second-line solution (after steroid or biologic treatments) rather than a first-line solution.

A significant uncertainty for plans is whether the market for high-cost AD drugs will expand, or whether some patients who are taking Dupixent will move over to one of the newer medications. What is clear is that, even with these new options, the treatment for moderate to severe AD continues to be expensive.

[6] https://www.newswire.ca/news-releases/amd-awareness-month-sheds-light-on-the-leading-cause-of-severe-vision-loss-in-older-adults-873116846.html
[7] https://www.epso.ca/vision-health/eye-conditions/retinal-diseases/amd/amd-treatments/
[8] https://www.fiercepharma.com/pharma/eylea-may-beat-lucentis-on-price-but-what-of-avastin
[9] https://www.roche.com/media/releases/med-cor-2021-02-12.htm
[10] https://dermatology.ca/public-patients/skin/eczema/
[11] https://www.aafa.org/atopic-dermatitis-in-america/
[12] https://www.ncbi.nlm.nih.gov/books/NBK539153/
[13] https://www.cadth.ca/sites/default/files/DRR/2021/SR0689 Adtralza Draft CADTH Recommendation (with redactions) November 4%2C%202021_for posting.pdf
[14] https://cadth.ca/sites/default/files/cdr/complete/SR0614 Rinvoq CDEC Final Recommendation February 6%2C%202020_for posting.pdf
[15] https://www.fda.gov/drugs/drug-safety-and-availability/fda-requires-warnings-about-increased-risk-serious-heart-related-events-cancer-blood-clots-and-death

Multiple sclerosis

Multiple sclerosis (MS) represents just 0.1 per cent of claims but 3.5 per cent of costs, which puts it among the top 10 drug categories by eligible cost, according to the 2021 TELUS Health Drug Data Trends & National Benchmarks report.

One development that may help reduce these costs is Health Canada's approval of 14 generic versions of Biogen's MS drug Tecfidera (dimethyl fumarate) in October 2021. Tecfidera costs about $23,000 annually,[16] so increased availability of generics could have a positive impact on plan costs.

Meanwhile, Biogen's Vumerity (diroximel fumarate) is expected to receive Health Canada approval soon and is likely to be offered at the same price as Tecfidera. Vumerity is being positioned as a next-generation version of Tecfidera with a better tolerability profile—in particular, reducing gastrointestinal side effects.

Specifically, a clinical trial conducted in 2020 found that patients receiving diroximel fumarate experienced less severe gastrointestinal events and fewer days of gastrointestinal symptoms than patients receiving dimethyl fumarate. They were also less likely to stop taking the medication.[17]

Vumerity may face an uphill battle for adoption in Canada in a landscape that already includes so many generic dimethyl fumarate options. Its effect on plan costs remains to be seen.

COVID-19

Researchers have developed a range of vaccines and treatments for COVID-19 in just two years. To date, these haven't had an impact on plan costs as they are being provided through public pandemic efforts. That is likely to remain the case in the near term, given that the federal government has placed significant orders for two antiviral pills destined for use outside hospitals. Furthermore, new options to vaccinate against and treat COVID-19 have the potential to keep plan members safer and to reduce the amount of time they are away from work recovering from COVID-19. This will clearly affect plan member outcomes in a positive way.

Health Canada has approved COVID-19 vaccines from Pfizer (Comirnaty), Moderna (Spikevax), AstraZeneca (Vaxzevria), Janssen/Johnson & Johnson (Janssen) and, most recently, Novavax (Nuvaxovid) and Medicago (Covifenz). It is currently reviewing two more: Sanofi Pasteur's recombinant protein-based vaccine and Vaccigen's whole virion inactivated coronavirus vaccine.

Six biologic monoclonal antibody treatments, generally administered intravenously in a hospital setting, are also under review at Health Canada. Three are already authorized under an interim order but are seeking full approval: GlaxoSmithKline's sotrovimab, Eli Lilly's bamlanivimab and Regeneron's casirivimab + imdevimab cocktail. However, of these, only sotrovimab has proven to be effective against the Omicron variant and there are concerns about its efficacy against the BA.2 subvariant.[18] The other three under review are AstraZeneca's cilgavimab + tixagevimab, Eli Lilly's etesevimab and Celltrion's regdanvimab.

Potential game changers are antiviral pills that patients can take at home. Pfizer's Paxlovid (combining nirmatrelvir and ritonavir), approved in January 2022, had impressive clinical trial results, reducing the risk of hospitalization or death by 89 per cent compared to placebo among high-risk adults with COVID-19 who had not been hospitalized.[19] It appears to work well against the Omicron variant. Merck's molnupiravir, approved by the FDA, was still under review by Health Canada at the time of publication.

[16] https://mssociety.ca/managing-ms/treatments/medications/disease-modifying-therapies-dmts/tecfidera
[17] https://pubmed.ncbi.nlm.nih.gov/31953790/
[18] https://www.aha.org/news/headline/2022-03-29-fda-sotrovimab-no-longer-authorized-where-ba2-subvariant-predominates
[19] https://www.pfizer.com/news/press-release/press-release-detail/pfizers-novel-covid-19-oral-antiviral-treatment-candidate

Generics

In addition to the Tecfidera generics discussed in relation to MS, one other significant medication now has generic alternatives.

Takeda's Intuniv (guanfacine hydrochloride), a therapy for attention deficit hyperactivity disorder (ADHD), went generic in January 2022. This is one of the more expensive ADHD therapies, with a cost above $3,500 annually for the highest (7 mg) dose.[20] It was also one of the few remaining single-source ADHD therapies. With ADHD affecting an estimated five to nine per cent of children and three to five per cent of adults,[21] this generic has the potential to make a difference to plan costs.

Several other generics are on the horizon. It's likely that by the end of 2022, generics will be available for Otezla (apremilast), Firazyr (icatibant) and Xeljanz (tofacitinib). Note that a more recent product, Xeljanz XR, remains under patent.

Amgen's Otezla is an oral treatment for moderate to severe plaque psoriasis when conventional systemic therapy hasn't worked or is contraindicated. Plaque psoriasis is responsible for about 90 per cent of psoriasis cases and causes chronic skin inflammation for about 900,000 Canadians.[22]

Takeda's Firazyr is an injectable treatment for acute attacks of hereditary angioedema. It is a high-cost specialty drug for a condition that causes often unpredictable painful swelling in an estimated one in 50,000 people.[23]

Pfizer's Xeljanz is a second-line oral treatment for moderate to severe rheumatoid arthritis, active psoriatic arthritis and active ulcerative colitis. Xeljanz is a JAK inhibitor, so safety concerns may limit the use of both the name-brand and generic molecules going forward.

Biosimilars

Beyond the Lucentis biosimilar for macular degeneration covered earlier, the biggest biosimilar story this year will be the continued rollout of switching programs. In February 2022, Nova Scotia became the sixth Canadian province/territory to introduce a biosimilar switching program, following British Columbia, Alberta, New Brunswick, Quebec and the Northwest Territories. Ontario's Cabinet announced the approval of a program in late February 2020, but it stalled with the arrival of the pandemic.

The 2021 TELUS Health Drug Data Trends & National Benchmarks report analyzed the impact of British Columbia's program, announced in May 2019. It found that, compared to a January 2019 national baseline, the cost per claimant in B.C. dropped to 88 per cent just one month later and to 67 per cent by the end of 2020. In the rest of Canada, the cost per claimant rose to 106 per cent in June 2019 and to 118 per cent by the end of 2020. So, implementation of biosimilar switching programs in more provinces and territories will undoubtedly have an impact on plans within those jurisdictions.

Finally, biosimilars for AbbVie's Humira (adalimumab), Genentech's Avastin (bevacizumab) and Novo Nordisk's NovoLog (insulin aspart) are currently awaiting Health Canada approval. However, since biosimilars for each of these molecules already exist, approval is not expected to have a significant effect on plan costs.

[20] https://www2.gov.bc.ca/assets/gov/health/health-drug-coverage/pharmacare/adhd-3471-info.pdf
[21] https://caddac.ca/understanding-adhd/in-general/
[22] https://www.newswire.ca/news-releases/protezla-apremilast-tablets-first-in-a-new-class-of-oral-treatment-receives-health-canada-approval-for-plaque-psoriasis-516432131.html
[23] https://aacijournal.biomedcentral.com/articles/10.1186/s13223-019-0376-8

Conclusion

This year's report focuses on a therapeutic area not often considered a cost driver in private plans (Alzheimer's disease), the rapid expansion of a market with a number of high-cost options (AD), and two areas where manufacturers are introducing new products to manage the loss of market exclusivity of past products (MS and AMD).

The expected entry of high-cost specialty drugs into the Alzheimer's disease market that are targeted to younger people of potential working age represents an entirely new cost for private payers.

Product life cycle management strategies such as those we see with Vumerity and Susvimo are not new. While they may not mean "net new" costs to private payers, they do carry the threat of lost savings associated with expected generic and biosimilar entries in those spaces. These new agents may offer benefits to some patients, and strategies such as prior authorization can be used to help control associated costs.

The AD space is a good example of how the drug pipeline can change. The arrival of oral agents was initially seen as competition for an established injectable product. However, safety concerns over another drug in the class have relegated these newer options to a later stage in therapy, largely preserving the status quo.

While COVID drugs have been provided to date by public plans and have not yet had an impact on private payers, the pandemic has essentially affected all areas of our lives, and a look at this unique piece of the pipeline demonstrates continued strides against COVID-19 as we move closer to a "new normal."

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