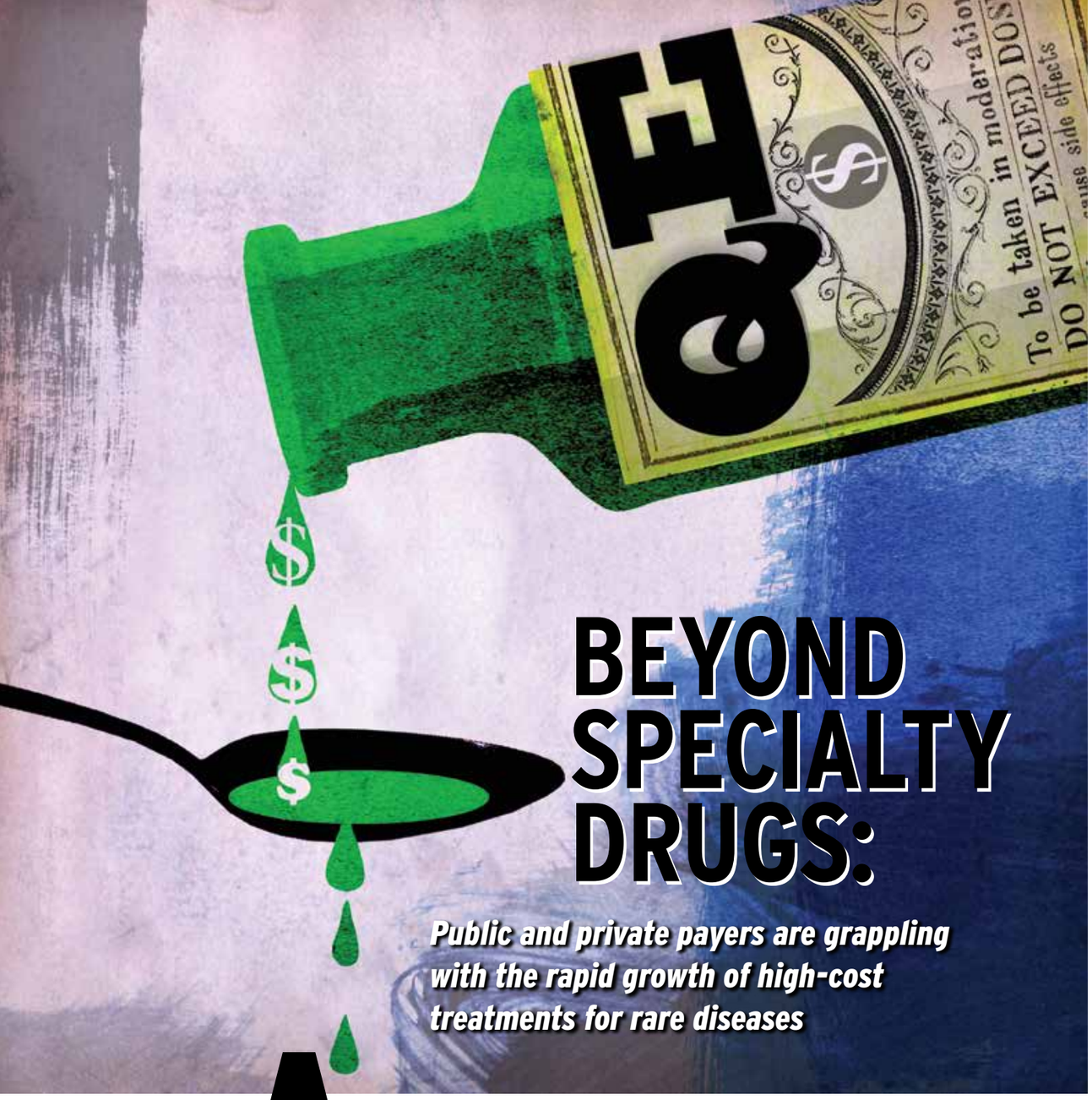

BEYOND SPECIALTY DRUGS:

Public and private payers are grappling with the rapid growth of high-cost treatments for rare diseases

By *Jann Lee*

A year ago, the Association of Ontario Midwives Benefits Trust received its highest drug claim ever at $55,000 for a 12-week treatment of Harvoni, which treats hepatitis C.

The plan deliberated whether it would fund the drug but it ultimately decided not to.

"It was a very difficult decision," says Nicole Mellin, executive director at the benefits trust.

Mellin says she was disappointed the benefits trust couldn't help the plan member, but the drug was not only absent from the plan's formulary, it also surpassed its $10,000 threshold for individual claims. If the benefits trust had funded the drug, it would have had to use its drug pooling mechanism, says Mellin.

And while the benefits trust already turns to its drug pool to fund some specialty drugs, Mellin says she has yet to encounter a claim for orphan drugs, a more expensive class of medications that has been piquing the interest of the benefits industry.

The growing impact of orphan drugs is "very concerning," says Mellin, noting the benefits trust has been working with its insurer and its benefits consultant to discuss how it can mitigate the risks of future claims for high-cost drugs.

> ***"If the cost of the drug is half a million dollars per year or a million dollars per year, you can see that maybe nobody but Bill Gates or a few others can afford that.***

Unlike medications for common diseases, orphan drugs treat rare conditions that affect a very small population, says Larry Lynd, a professor with the faculty of pharmaceutical sciences at the University of British Columbia. He notes there are about 7,000 identified rare diseases, many of which lack treatments. About 80 per cent of rare diseases are genetically linked and many of the patients are children. In some instances, the patients are adults who learn about a rare condition later in life.

With advanced science and technological tools at their disposal, companies are finding it easier to develop new treatments for rare diseases, once they're able to detect a specific genetic aberration, says Lynd. "We're seeing more and more orphan drugs on the pipeline . . .. I haven't seen a number of exactly how many orphan drugs there are today, but it's fairly dynamic. It's changing all the time."

While orphan drugs are bringing hope to patients suffering from life-changing conditions, affordability is a significant concern, says Lynd. He notes many of the drugs cost more than $100,000 per year, with the price reaching $1 million for some medications. "If the cost of the drug is half a million dollars per year or a million dollars per year, you can see that maybe nobody but Bill Gates or a few others can afford that. The only way these drugs will get to the patients is if they're covered by some payer, whether it be public or private," says Lynd.

'Accumulation' of drugs a concern

Orphan drugs make up a small percentage of total drug claims, but the influx of new products is a concern for benefits providers, says Jean-Michel Lavoie, assistant vice-president of product development and group benefits at Sun Life Financial. "The issue is it's not just a couple of drugs anymore . . .. It's the accumulation of all of those drugs that make it a concern."

Sun Life has been tracking orphan-drug claims since 2011, and the numbers have gone up every year, according to Lavoie. By the beginning of 2017, the number of claims was double the figures for 2011-12.

Plan sponsors that receive a claim for an orphan drug are in a difficult position, says Sandra Ventin, associate vice-president at Accompass Inc. "They're always highly emotionally charged decisions, because over 95 per cent of the time, these drugs represent themselves as a life-or-death situation. For a plan sponsor that wants to be the employer of choice, they're being put in an

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ALEXION CHALLENGED OVER SOLIRIS PRICING

In a long-running case, the Patented Medicine Prices Review Board has been conducting hearings into whether Alexion Pharmaceuticals Inc. has been selling the drug Soliris at an excessive price to Canadians. According to the federal regulator of drug prices, the annual cost for Soliris is more than half a million dollars. Board staff allege Alexion has been selling the product to Canadians at the highest international price among comparator countries. The regulator is seeking an order that would require the company to stop selling it at the current cost of $224.73 per millilitre and offset the excess revenues it has generated from sales.

The company is vowing to fight the allegations, says John Haslam, general manager at Alexion Pharma Canada Corp. He says the company set the price for Soliris in 2009 in accordance with the federal regulator's guidelines and was compliant until 2011.

The price changed in 2012-13 due to the booming oil sector, which helped inflate the Canadian dollar, says Haslam. "So what happened was that our price went above comparative countries during that time . . .. The price now is back because the Canadian dollar dropped down and is back within guidelines. So this was something that was beyond our control. It was an exchange-rate issue."

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extremely awkward position of saying yes or no."

While large employers typically have administrative services-only contracts and may be able to shoulder more risk, insurance companies take on more of the responsibility when it comes to fully insured smaller companies, says Ventin. But regardless of the arrangement, she notes orphan-drug claims are a possibility and can have a significant effect on any employer.

The challenge arises when employers have no choice but to implement extreme measures, such as introducing caps or eliminating coverage altogether, says Stephen Frank, senior vice-president of policy at the Canadian Life and Health Insurance Association.

"You're seeing some instances of plans opting not to cover these rare disease drugs anymore. And when you start to have a market that's considering or implementing things like carving out certain types of drugs in their coverage or putting caps in place, all of those things are really blunt tools that don't benefit the patient and don't really benefit the system in the long run. So we're concerned that that not be allowed to happen in a big way."

Developing an orphan-drug framework

Patients facing a denial of funding by plan sponsors may not fare any better with provincial drug plans, especially given the lack of co-ordination between private and public drug programs in Canada, says John-Paul Dowson, managing director at Roubaix Strategies Inc. "There's no guarantee the public plan is covering the same drug or, if they do cover the drug, there's no guarantee it will be covered under the same type of criteria or that it'll be covered in the same time."

When it comes to reimbursement for orphan drugs, the assumption is that private plans are the first payer and provincial health plans come next, says Dowson. He notes each province has a public formulary that lists the drugs it will cover under various drug programs, which usually support seniors and other groups. Some provinces, including British Columbia, Alberta, Saskatchewan, Ontario and New Brunswick, have programs specific to rare diseases that aim to provide reimbursement under certain conditions, according to the Canadian Agency for Drugs and Technologies in Health.

Whether patients will get coverage really depends on the province, says Dowson. In the case of British Columbia, while it has a program that addresses drugs for rare diseases, it makes decisions about coverage on a case-by-case basis, he notes.

Given the current patchwork of programs, Canada needs a national framework around orphan drugs so there's a clear process for drug evaluation and reimbursement, says Lynd. Not only would the policy ensure equal treatment for all Canadians, it would also make it easier for public payers to communicate and work with private plans, he says.

Indeed, Health Canada is working on a regulatory framework for orphan drugs, but the purpose will be to encourage their development and increase their availability in the Canadian market, according to the department's website.

The proposed framework doesn't help benefits providers because they'll face even more uncertainty about which drugs to cover, says Frank. "What we want to avoid are situations where you have a very expensive drug where the evidence around its effectiveness isn't conclusive yet," he says.

"And I think that's one of the biggest issues: We don't want to be paying for drugs if we don't know they're going to work. And if that situation were to happen, payers, both public and private, start to look like they're subsidizing clinical trials."

While the regulatory framework will make it easier for Canadians to access orphan drugs, it doesn't address whether the products are affordable in the first place, says Doug Coyle, professor and director of the school of epidemiology and public health at the University of Ottawa. The potential changes from Health Canada will create more confusion around orphan drugs because they'll drive more of them onto the market for payers to evaluate, he notes.

A PRIMER ON SOME ORPHAN DRUGS AND THE DISEASES THEY TREAT

Currently, the U.S. Food and Drug Administration has about 587 medicines classified as orphan drugs. While Health Canada doesn't have an official list, it has reviewed and approved the orphan drugs below. The costs aren't definitive because specific pricing information for drugs is confidential, according to the Patented Medicine Prices Review Board.

Strensiq treats patients with pediatric-onset hypophosphatasia, a disease that can lead to the destruction and deformity of bones, along with other complications.

Cost: $286,416 to $2,545,920 per year, depending on the patient's weight

Elaprase treats patients with Hunter syndrome, a rare lysosomal storage disease that causes people to experience growth delay, joint stiffness and coarsening of facial features, according to Health Canada. In severe cases, patients can experience respiratory and cardiac problems, liver and spleen enlargement and neurological deficits.

Estimated cost: $1 million per year

Vimizim treats patients with Morquio A syndrome, an autosomal recessive genetic disorder caused by the deficiency of a specific enzyme due to gene mutations, according to Health Canada. The U.S. Food and Drug Administration notes the absence of the enzyme leads to problems with bone development, growth and mobility.

Estimated cost: $1 million per year

Soliris treats patients with paroxysmal nocturnal haemoglobinuria, a disease that ruptures and destroys red blood cells, and atypical hemolytic uremic syndrome, a disease marked by blood clots in small vessels, according to Health Canada. Patients with either disease can experience severe, life-threatening symptoms including anemia, fatigue, pain, blood clots and renal failure.

Estimated cost: $500,000 to $750,000 per year, depending on the patient's weight

Kalydeco and Orkambi are oral treatments for specific types of cystic fibrosis, according to Health Canada. Patients with cystic fibrosis may experience breathing problems, gastrointestinal abnormalities, liver dysfunction, pancreatic disease and reproductive abnormalities.

Cost: $306,000 per year for Kalydeco and $249,000 for Orkambi

LIMITATIONS OF ORPHAN DRUGS

Not curative: While orphan drugs can mitigate chronic and debilitating symptoms, they don't cure the disease and patients may need to be on the treatment for life, notes the University of British Columbia's Larry Lynd.

Limited scientific data: There's little data on the long-term effects of orphan drugs, says Lynd. "We have very small sample sizes and very small trials upon which to base our assessment on whether the drug is efficacious."

Side-effects: Because orphan drugs treat rare and complex diseases, their potential side-effects remain unclear, says Helen Stevenson, founder, president and chief executive officer at the Reformulary Group Inc. "The other side of these drugs is that they're very powerful and people could have severe reactions to infusions. It's not just popping a pill and feeling normal," she says, noting many of the drugs require special handling and administration.

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Justifying the high costs

Plan sponsors, the pan-Canadian Pharmaceutical Alliance and the Patented Medicine Prices Review Board all need to study and assess the value of orphan drugs, says Lavoie. "From my perspective, pharmaceutical companies have a corporate social responsibility. What's the justification for the price they're charging? There's not a consensus as to what a drug is really worth."

Many factors affect pricing, including the risk that pharmaceutical companies take in developing and bringing the drugs to market, says John Haslam, general manager at Alexion Pharma Canada Corp. "You look at these ultra-rare diseases and ultra-rare drugs with very few patients out there and, when you look at the clinical trials and approvals for clinical trials, it's very complicated and goes across a number of countries just to get enough patients. There's really no well-established road map for regulatory approval or manufacturing, so costs are very complicated."

> ***"We want to have one national approach to get the best price for everyone.***

U.S. manufacturers benefit from government financial incentives to develop drugs for rare diseases, according to *Kaiser Health News*. The nonprofit news service notes that under the U.S. Orphan Drug Act, manufacturers that receive an orphan-drug designation can get a fee waiver for registering the product for approval; a 50 per cent tax credit for all clinical trials related to drug development; support from the U.S. Food and Drug Administration's rare-disease program while developing and testing the drug; and seven years of guaranteed exclusivity in the market.

As well, some pharmaceutical companies incur lower development costs because they don't invest in the early stages of drug development, says Lynd. He points to Kalydeco, a drug that treats cystic fibrosis. "The Cystic Fibrosis Foundation actually funded the early identification and development of Kalydeco, and then another company came along and bought the patent from the foundation and then continued through the final phases and made the application to the regulator to get market approval, market authorization and then brought the drug to market."

While the companies aren't skipping steps in research and development, they're able to save costs by continuing the work already done by other organizations, notes Lynd. "There's a potential to make 1.7 to two times the return on your investment on an orphan drug relative to a non-orphan drug," he says.

As a result, many companies are shifting to developing orphan drugs because of the potential for greater returns, says Lynd. "That's really the environment we're working in where more pharmaceuticals are moving, which again is really going to just continue to create pressure on payers as more and more drugs get developed."

While there's no easy solution for public and private payers that want to provide benefits to their members, collaboration is essential in order to keep the costs sustainable, says Frank, suggesting the pan-Canadian Pharmaceutical Alliance should include private insurance companies when it negotiates prices with drug companies. "It doesn't make sense for Canada to have multiple buying blocks. We want to have one national approach to get the best price for everyone."

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