

» Tapping in to the drug pipeline

Back in the winter 2015 issue of *Follow the Script*, we outlined the drug development process and how new drugs come to market – this is sometimes called the “drug pipeline.” With so many new drugs – particularly expensive specialty drugs – on the horizon, we thought this was a good time to revisit this topic and explain how GSC, both a benefits carrier and pharmacy benefits manager, learns about new drugs coming to market and how we use that information to develop our policies and strategies.

Discovering what's coming

It's no secret that drug spending has risen dramatically in recent years, and there's no sign that the volume of costly new specialty drugs is going to decrease anytime soon. It's therefore important for GSC and its community of plan sponsors and advisors to know what's coming and how it will fit into an overall drug strategy. How do we do this?

1. Monitoring the drug pipeline

GSC's Pharmacy Strategy department keeps an eye on the drug pipeline and manages the information about the coming drugs. This means we seek out information about drugs under development, including clinical trials that are upcoming or underway, in Canada and internationally, especially in the United States and the European Union.

While we do monitor individual drugs, we are particularly interested in development trends in specific therapeutic areas. Those trends tend to forecast a coming wave of potential treatments that we need to be aware of in our strategic planning.

Knowing what's happening in other countries can be particularly useful. Once we identify a drug as likely to be approved in another jurisdiction, we work with the manufacturer of that product to better understand the potential timing of entry to the Canadian market.

As there's no single source that describes drugs under development, we refer to many sources, for example:

- **Academy of Managed Care Pharmacy** distributes a daily newsletter that contains information about new drugs.
- **Medscape News** outlines information on drug approvals by the U.S. Food and Drug Administration (FDA), new drugs in development, new indications for existing drugs, and the status of clinical trials.
- **American Pharmacists Association** lists new approvals by the FDA.
- **Health Canada** maintains databases of drugs under review and Canadian clinical trials.
- **Industry conferences** offer exposure to other pharmacy professionals, drug company information, researchers, etc.

2. Forecasting the impact

Once we're reasonably sure that a particular drug is likely to come to market in Canada, we swing into forecasting mode and prepare a number of impact analyses for GSC's internal use. We examine details such as the cost of the drug, the potential number of patients it could treat, and whether this new drug will displace any existing therapies. In this process, we also look for "indicator" drug claims – patients who are currently using alternative therapies that may result in a switch to the new pipeline drug. Analysing this information helps us determine the impact any new drug will have on our customers' plans. It also helps in anticipating potential placement of the new products on our formularies. Being aware of the full picture of new therapies coming to market allows us to make strategic decisions around timing and listing criteria.

Drug Early Warning (DEW) system

To help us monitor both the drug pipeline and to forecast the likely impact of specific medications, GSC uses a tool called the DEW system. This online dashboard uses GSC data to help us more efficiently assess the potential impact of specialty drugs on our drug benefits plans.

The DEW dashboard provides:

- Information on new specialty drugs in development and new indications for existing drugs
- Expected costs of the new drugs
- Business intelligence, such as spending growth rates

Drug Early Warning (DEW) System™ and DEW™ are trademarks of Reformulary Group Inc.

3. Operational planning

Once a specialty drug is approved by Health Canada, GSC has to plan how to incorporate it into our drug plans and determine whether it will impact our pricing (for example, stop loss). We typically receive a full clinical submission from the manufacturer of the product which includes clinical trial data, recommendations by other health technology assessment agencies, expected budget impact analyses, and other information. Based on this information, as well as a broader scan of evaluations by the Canadian Agency for Drugs and Technologies in Health (CADTH) and other agencies, GSC reviews the product through our internal Pharmacy and Therapeutics Committee. In developing our listing criteria, we take a number of factors into consideration:

- Are any special or updated processes or policies required?
- Is there anything we need to communicate to pharmacy providers or our clients?
- Will the new drug be included in the GSC prior authorization process and/or our specialty drug preferred pharmacy network?
- Where does the drug fit in to the treatment paradigm, i.e., does it impact other therapies?
- Can partnerships be made with the manufacturer for preferred pricing and/or risk sharing agreements?

GSC's drug pipeline process in action

Follow the Script featured the topics of biologic drugs and biosimilars (a.k.a. subsequent-entry biologics or SEBs) in a couple of previous editions. Now you have learned how GSC followed the process described above to determine our strategy for these expensive drugs as they arrived on the market in Canada.

Biologic drug therapies have been a mainstay of treatment for a number of serious medical conditions, including Crohn's disease, rheumatoid arthritis, and several others. More recently we saw the emergence of less expensive biosimilar drugs coming to market in jurisdictions around the world. By monitoring the arrival of biosimilars in Europe – how they were received by the medical community and how the market share for them grew – we were able to predict the timing and impact on the Canadian market.

While other carriers were eager to pursue pricing agreements with originator biologic manufacturers, GSC took a longer-term, strategic view of the marketplace and instead established a new policy that made biosimilars the preferred products under our formularies. Our approach ensures that plan members starting on a new drug therapy, who can safely and appropriately use a biosimilar medication, will be required to do so to receive reimbursement. We were strongly encouraged when public drug plans across Canada followed in our footsteps and similarly made biosimilars the preferred option for patients starting biologic therapy.

What's coming down the pipe?

Here are two trends we're watching as we monitor the drug pipeline.

Oncology (cancer)

Cancer continues to be a difficult disease to treat. While some forms of cancer are now considered curable, others have few effective treatment options available. We anticipate that oncology drugs, and in particular a new type of treatment called "immuno-oncology," will be a huge growth area going forward. Immuno-oncology drugs help the body's own immune system fight off cancer and have shown tremendous promise in not only delaying the growth of cancer but in some cases also effectively eradicating it from the body.

NASH (non-alcoholic steatohepatitis)

NASH is a specific type of fatty liver disease where the accumulation of fat is associated with inflammation and damage to the liver. It's very common in North America, as risk factors include obesity, type 2 diabetes, and high blood pressure – all of which are prevalent among Canadians. It can be estimated that as many as 1.75 million Canadians may suffer from some form of NASH. There is currently no approved treatment other than lifestyle change; however, since significant advances have recently been made in understanding how the condition starts and progresses, several large pharmaceutical companies now have drugs in development to treat NASH, with the expected market entry in 2019 or 2020.

Stay tuned as these trends continue to develop.

BEHIND THE COUNTER



Quitting smoking sounds easy but it's not that simple

Smoking is a major factor in cardiovascular disease, diabetes, and several forms of cancer and has a negative impact on the health of many plan members. This issue we talk to GSC pharmacist Leila Mandlsohn about addiction, quitting smoking, and how pharmacists can help.

Follow the Script: Welcome back to *Follow the Script*, Leila. In our winter 2016 issue, we talked to your colleague Chris Leung about addiction and opioids, so let's start there. Is addiction the biggest challenge when someone wants to quit smoking?

Leila: Yes, addiction by far is the biggest challenge for anyone who wants to quit smoking. I'm sure that Chris told you that addiction is a complicated problem – it involves environmental, genetic, and behavioural factors. Addictive substances, like nicotine in tobacco, trigger the release of chemicals in the brain that cause pleasure – people get positive reinforcement or a “reward.”

FtS: Is there any difference in being addicted to smoking or alcohol or food? Is it all basically the same thing only a different substance?

Leila: The same things apply to every addiction; whether it's smoking, alcohol, or drugs, there's that underlying psychological component that's involved in all of them. It's a huge challenge. There's some research that suggests that there's the same kind of positive reinforcement triggered in the brain when some people consume sugar or certain types of food.

FtS: We've been talking about ingesting substances, but would addiction be the same with something like gambling? Or is that different.

Leila: You say *addiction* and you think drugs, alcohol, cigarettes. Addiction in itself is such a complex process – but it goes beyond those substances. There's a component of how prone a person is to addiction. A person who's genetically susceptible to addiction likely can develop a problem with a compulsive behaviour. Since the reward system in the brain is reinforced by things like gambling, that seems to be the same as being addicted to a substance. We're also reading a lot about being addicted to your phone – you get that new message on your phone and that gives you the positive feedback. It's all about the chemicals released in your brain in response to whatever the stimulus is and the positive reward mechanism.

FtS: So, back to smoking, it makes the smoker feel good?

Leila: Well, in addition to the physical dependence that occurs, there's also the psychological aspect of it – both processes work together. Smoking often becomes a coping mechanism to deal with other stuff. Let's say you're struggling with stress – whether it's at work or at home – and you go to that behaviour to sort of escape, right? Someone's under stress, so they go and smoke. You also hear a lot about people eating as an escape from whatever they're dealing with. Same thing with alcohol.

FtS: Then if the stress in someone's life doesn't disappear, how does that person stop smoking?

Leila: They need to learn other coping mechanisms – something else to help deal with stress. I think one of the reasons people fail when they try to quit smoking is that they don't have the ability or the resources or the support to be able to find what it is they need to do to compensate. They no longer have the cigarette to go and escape to... so how are they going to deal with the stress? A lot of people, they stop smoking, but then they're eating more and gain weight. They could just be going from one addiction and coping mechanism to another. There needs to be something else. Is it going to be meditation? Is it going to be mindfulness or reading a book? I think getting that kind of wide-ranging, thoughtful support is often what's missing.

FtS: Is that why we've always suggested that the best treatment for smoking cessation is a combination of the drugs and counselling?

Leila: Yes. We have effective drugs for smoking cessation, but access to the drugs can be a challenge because they're not readily available across all benefits plans. Some plans excluded them over the years or placed severe limitations on reimbursement because they were seen as "lifestyle drugs." So making the drugs available certainly helps with the physical dependence on tobacco, but a drug doesn't replace the behavioural dependence. Having access to counselling support to navigate through the process is also often necessary for people to ultimately quit smoking.

FtS: So we're paying pharmacists to provide smoking cessation programs but what you're describing sounds like the job of a psychologist. Are pharmacists equipped to counsel about replacing stress relief with something else?

Leila: They are because the smoking cessation training programs for pharmacists incorporate all the required messaging. The programs teach about assessing the patients to see where they are in the stages of change. Are they ready to make the change? Or are they just contemplating a change but not ready to make it? If they're not ready to quit, they can talk about it again in a few months.

There's a lot of education offered to pharmacists about communicating with patients in general, not just related to smoking cessation. For instance, there's training on motivational interviewing – asking the questions in a way that you're not telling the person what they need to do or how to go about it; you're helping them get to that place themselves.

If you're a pharmacist who provides a smoking cessation program regularly, you can get really good at it. If you're a pharmacist who does it ad hoc, communication of that nature can be challenging. Coaching patients is a skill that you have to develop.

FtS: But isn't it hard to have a volume of patients at any one location to get good at it or are there some pharmacies that specialize in this?

Leila: There are definitely some pharmacies that specialize. There are some that have a very strong smoking cessation program in their community and they're known for it. For example, Jane Ling, a pharmacist at Lovell Drugs in Oshawa, specializes in smoking cessation. She's done all the training and is very experienced. The program is promoted in the store and on the pharmacy's website. In the pharmacy's workflow, when a person drops off the prescription, the technician or pharmacist enquires about the patient's smoking status to assess whether the person should be channeled towards the program. Jane has also started an organization called Pharmacists for a Smoke Free Canada to promote the role of pharmacists in smoking cessation.

FtS: Tell us about GSC's smoking cessation program.

Leila: GSC's smoking cessation program has been around for over a decade, but we revamped it in early 2016 to include more flexibility for plan members. With smoking being the leading cause of preventable death in Canada and a risk factor for many of the chronic conditions we see in plan members, it made sense for GSC to revisit the topic. We've promoted the program to plan sponsors and pharmacists, and we've been encouraging pharmacists to do the training, which is available through their provincial associations. Since there are many smoking cessation programs around, including some sponsored by the provincial health plans, pharmacies are hearing the message from multiple sources and that drives awareness.



In 2017, most plan sponsors have now included the smoking cessation program in their plans, so it's widely available across Canada to GSC plan members, and we're seeing more and more claims from all provinces. We can also see that most people who start the program complete it which means they are more likely to be successful in quitting smoking.



FtS: And that's good for everyone. As always, Leila, it's been great talking with you. Thanks for your time.

DRUG REVIEW AT GSC...

To give you an idea of what drugs might impact your benefits plan next, every quarter *Follow the Script* highlights some of the drugs recently reviewed by GSC’s Pharmacy and Therapeutic (P&T) Committee.

GSC CLASSIFICATION ¹	NEW DRUG ²	GENERAL INFORMATION	COST ³	COVERAGE DETAILS ⁴
RARE DISEASES				
Traditional; Specialty (Tier 5)	Pheburane™ (sodium phenylbutyrate)	<p>The urea cycle refers to the internal process, involving six enzymes, that is responsible for converting toxic nitrogen in the form of ammonia (a waste product of protein metabolism) into non-toxic urea for excretion from the body as urine. When a genetic mutation results in a deficiency in any of the enzymes, it is referred to as urea cycle disorder (UCD). Onset and severity of UCD are highly variable and dependent on the specific genetic mutation(s) involved and the amount of enzyme function remaining. In severe cases (little to no enzyme function), children typically show symptoms after the first 24 hours of life due to rising ammonia levels in the blood. If left untreated, the toxic ammonia accumulates and can reach the brain, resulting in brain damage, coma, and/or death. Patients with mild mutations can sometimes go undiagnosed into adulthood until a stressor (e.g., illness, high protein intake, excessive exercise, etc.) further interferes with enzyme function and causes high amounts of ammonia to accumulate. This can result in symptoms such as disorientation, confusion, or slurred speech. There is currently no cure; however, patients can be treated through dietary management to limit ammonia production, along with therapies that help remove ammonia from the bloodstream (nitrogen scavengers).⁵ The overall incidence of UCDs is estimated to be 1/35,000 live births.⁶</p> <p>Until recently, there were no Health Canada-approved treatment options for the management of UCD patients. The only way to access treatment was through Health Canada’s Special Access Program (SAP) which enabled patients to import Buphenyl® (sodium phenylbutyrate) from the United States. (Buphenyl® is a nitrogen scavenger that prevents ammonia formation.) With the availability of Pheburane, the first treatment option to be approved by Health Canada for UCD, patients no longer need to access treatment through the SAP.</p> <p>Pheburane was approved for the treatment of UCD as adjunctive therapy (to dietary protein restriction and/or dietary supplementation) in: the chronic management of UCD (involving three specific enzymatic deficiencies); neonatal-onset presentation (complete enzyme deficiencies) within the first 28 days of life; and late-onset disease (partial enzyme deficiencies) presenting after the first month of life in those with a history of hyperammonemic encephalopathy (high levels of ammonia in the brain).</p> <p>Pheburane is available as coated granules and is administered orally based on weight (in those less than 20 kg) or body surface area (for those weighing more than 20 kg).⁷</p>	<p>\$\$\$\$\$</p> <p>Approximately \$58,000 – \$76,000 per year</p>	<p>→ Specialty drug PPN</p> <p>→ Requires prior approval</p>

GSC CLASSIFICATION ¹	NEW DRUG ²	GENERAL INFORMATION	COST ³	COVERAGE DETAILS ⁴
Traditional; Specialty (Tier 5)	Ravicti™ (glycerol phenylbutyrate)	<p>Ravicti, similar to Pheburane, is a nitrogen scavenger approved for the treatment of urea cycle disorder (UCD). However, in contrast to Pheburane, Ravicti was approved by Health Canada for the chronic management of UCD for patients age two or older who cannot be managed by dietary protein restriction and/or amino acid supplementation alone.</p> <p>Prior to the availability of Ravicti, the standard treatment was with sodium phenylbutyrate which was limited to the treatment of specific UCD enzymatic deficiencies and certain populations. Ravicti now offers a new treatment option for an unmet need. Ravicti is also available in liquid form so patients may experience improved tolerability and find it easier to administer due to reduced drug volume; plus it is odourless and tasteless.</p> <p>Ravicti is administered orally daily based on a body surface area.⁷</p>	<p>\$\$\$\$\$</p> <p>Approximately \$140,000 – \$350,000 per year</p>	<p>→ Specialty drug PPN</p> <p>→ Requires prior approval</p>
Biologic; Specialty (Tier 5)	Revestive™ (teduglutide)	<p>Short bowel syndrome (SBS) is a rare condition that refers to the functional or anatomic loss of extensive segments of the intestine so that absorptive function and capacity is severely compromised. Common causes of SBS include resection due to Crohn's disease, cancer, or radiation.⁸ As a result, some patients are unable to absorb adequate nutrients from the food they eat and can experience malabsorption, malnutrition, diarrhea, and electrolyte and fluid abnormalities. In severe cases of SBS, proper nutrition may not be possible without supplementation administered via the parenteral route (bypassing the normal digestion in the stomach and bowel). Although parenteral support (PS) may supply basic nutrition and fluid requirements, long-term use is associated with decreased quality of life and potentially life-threatening complications. Additionally, currently available treatment options simply manage patients' symptoms (e.g., diarrhea) and do not address the underlying intestinal malabsorption.</p> <p>Glucagon-like peptide 2 (GLP-2) is a naturally occurring peptide secreted by the lower intestinal tract which works by improving the intestine's absorptive capacity.⁹ Revestive, a GLP-2 analog, is the first targeted biologic therapy approved in Canada for the treatment of adults with SBS who are dependent on PS. Revestive offers a new treatment option for SBS that may help reduce the patient's dependency on PS.</p> <p>It is administered by injection once daily based on a patient's weight.</p>	<p>\$\$\$\$\$</p> <p>Approximately \$330,000 per year</p>	<p>→ Specialty drug PPN</p> <p>→ Requires prior approval</p>

Notes:

¹Traditional generally refers to small molecule compounds derived from chemical synthesis and also includes drugs not listed in Schedule D of the Food and Drugs Act; Biologic refers to drugs produced through biotechnology and listed in Schedule D of the Food and Drugs Act; Specialty (Tier 5) refers to drugs with an expected annual treatment cost of \$10,000 or more (certain drugs approaching the threshold may also be considered high cost if clinical evidence warrants).

²Brand (generic)

³Based on manufacturer list price, does not reflect pharmacy markup and dispensing fee. \$ <1,000; \$ 1,000–4,999; \$\$\$ 5,000–9,999; \$\$\$\$ 10,000–49,999; \$\$\$\$\$ ≥50,000

⁴Applicable to all formularies unless otherwise noted. PPN refers to GSC's preferred pharmacy network program.

⁵Urea Cycle Disorder, National Urea Cycle Disorder Foundation, <http://www.nucdf.org/ucd.htm>.

⁶Molecular Genetics and Metabolism 2013; 110: 179-180.

⁷Dosing based on weight or body surface area assumes a weight of 72 kg and body surface area of 1.75 m² respectively.

⁸Short-Bowel Syndrome, Medscape, <http://emedicine.medscape.com/article/193391-overview>

⁹Revestive, UptoDate, <https://www.uptodate.com/contents/teduglutide-drug-information?source=preview&search=Revestive&anchor=F16136098#F16136098>