20 SENSE

THE 20SENSE REPORT

Spotlight on the Canadian Specialty Pharmaceutical Market

October 2023
Issue 26

Has Managed Access Arrived in Canada?

The facts and figures behind managed access and outcomes-based agreements.

New processes based on managed access-like models are paving the way to more timely access.

NICE's Thomas Strong brings insights from a career of managed access in the UK to Canada.

By the *Numbers*

The road to timely and equitable access to specialty medications in Canada is still under construction. Fortunately, new processes based on managed access models and corresponding market access agreements are smoothing some of the bumps. While managed access means different things to different people, some commonly used definitions can help ground the discourse and give context to the pertinent facts and figures.

Managed access[1]:

Managed access schemes enable payers to fund innovative therapies while developing and gathering additional evidence, prior to finalizing the health technology assessment (HTA) and pricing negotiation processes. These schemes enable timely access for patients with a high unmet need for therapies that have evidence uncertainties.

Outcomes-based agreement (OBA)[2]:

An OBA is an innovative market access agreement between a manufacturer and a payer in which the manufacturer will issue a refund or rebate to the payer based on how well the therapy performs in a real-world patient population, measured against an agreed-upon, predefined set of benchmarks.

Real-world evidence (RWE)[3]:

Derived from real-world data (RWD) such as patient registries or claims data, RWE can be used to support managed access schemes and outcomes-based agreements. Implementing an RWE generation plan for new therapies with uncertain clinical trial evidence can help decision-makers to understand the value of the therapy.

By the Numbers

ACCESS INNOVATION IN CANADA

2

managed access-like processes that may enable timelier access to some novel therapies with a high unmet need; one is a time-limited HTA recommendation by CADTH and the other is a proposed temporary access process (pTAP) advised by the pCPA.[4,5]

1

calls for exploratory drug evaluation proposals from Quebec's HTA body, INESSS.[6]

10-20

Estimated number of "simple" OBAs in Canada, with payment models tied to clinical outcomes.[7]

6

Canadian public payers that have negotiated or implemented at least one OBA.[8]

ONGOING ACCESS CHALLENGES

24.6%

Among cancer drugs that made it to Phase 2 clinical trials, proportion that move ahead to Phase 3; once at Phase 3, 47.7% proceed to filing an application for a new drug/biologic.[11] Of all clinical phases, Phase 2 represents the largest hurdle in drug development.

19%

Proportion of submissions to CADTH's pan-Canadian Oncology Drug Review's Expert Review Committee supported by only Phase 2 evidence, as per a 2020 study.[10] Of these, 63% received a positive recommendation, as opposed to 82% for submissions with Phase 3 evidence.

> 1.5 YEARS

Time to access for new drugs in Canadian public plans. The delay from regulatory Notice of Compliance (NOC) to first listing is about 580 days for oncology therapies and 670 days for orphan drugs.[9]

65%

Average proportion of drugs approved in Canada that receive public reimbursement within 2 years.[9]

COMING SOON: NEW DRUGS THAT CALL FOR NEW THINKING

> 9,000

Number of new medicines at various stages of development in the 2022 pipeline, up from 8,500 the previous year.[12]

11%

Average annual increase in the number of pipeline drugs since 2018.[12]

30%

Proportion of 2022 pipeline drugs devoted to oncology – the top therapeutic area in the pipeline.[12]

31%

Medicines in Phase 3 clinical trials or pre-registration given an early orphan designation through the FDA or the EMA, attesting to the rising trend of orphan-designated new medicines.[12]

JURISDICTIONS LEADING THE WAY

31%

Difference between public coverage in top OECD countries (96%) vs Canada (65%) for drugs that treat unmet needs.[9]

1 OR MORE

Early access pathways already established in many countries including UK, France, Germany, Italy, and Australia.[13]

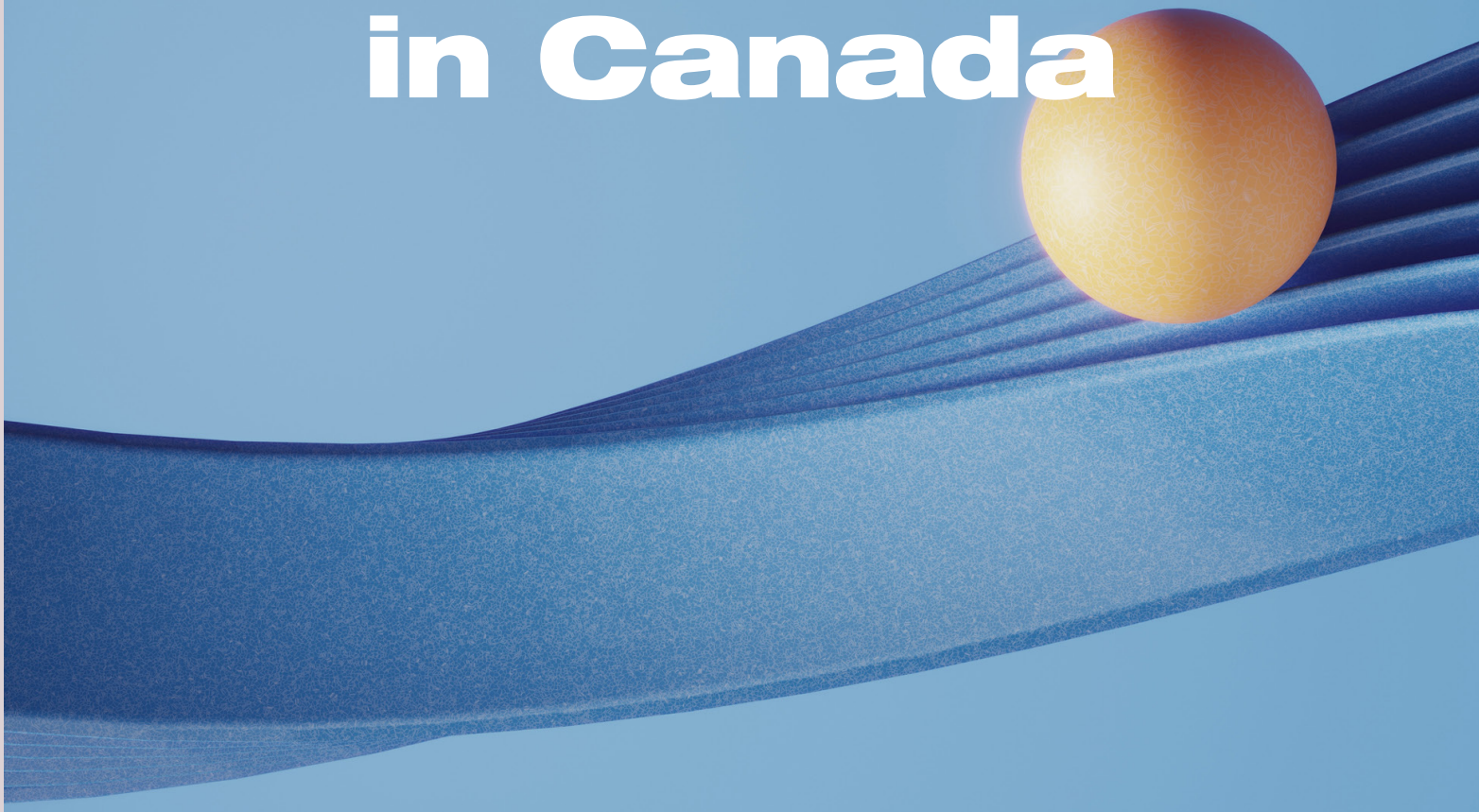
86%

Technologies recommended for routine use by the UK's NHS following a period of managed access.[14]

0

Days to access for 4 novel non-small cell lung cancer (NSCLC) therapies approved in the UK through Project Orbis and listed through early/managed access processes, enabling patients to receive the drugs an average of 7 months before routine listing.[8]

Update on Managed Access and OBAs in Canada



Managed access and outcomes-based agreements have moved from the visioning stage to the drawing board, with new and exciting implementation processes under way.

Managed access has crossed a threshold in Canada: from interesting solution to item on stakeholders' to-do lists. With drug innovation pouring in from all sides, and approval for promising medicines sometimes granted on the basis of incomplete but promising evidence, managed access has emerged as a fair and logical way to handle the deluge.

The surge of interest in managed access comes not a moment too soon, as many patients have been waiting – and waiting – for access to the treatments that could change their lives. Having travelled a long and hard road, often for years, they deserve to see change.

While managed access and outcomes-based agreements (OBAs) are hardly new ideas, Canadian policymakers have had understandable concerns about adapting them to the country's unique healthcare architecture. How exactly would managed access work in our multiple payer environment? Could our infrastructure handle the added complexity?

In the interim, other countries have demonstrated that these concepts can work – and more importantly, figured out *how* to make them work. They have shown us that managed access can take many forms, with components mixed and matched depending on a jurisdiction's needs and health system.

In Canada, it's no longer a question of whether to implement these schemas, but of when and how – with some exciting new policies and initiatives coming to fruition. Here, we explore what stakeholders are doing to make timelier access to novel therapies a reality across the country, and where managed access and OBAs fit in.

THE ACCESS GAP

Specialty pharmaceutical products often face an awkward hurdle in their life cycle: as highly promising and disruptive technologies, they may receive relatively fast approval, but patient access lags far behind. For months or even years, patients come up against an impenetrable wall, consigned to "look at, but not touch" the treatments that could change their lives.

Approval of promising and complex treatments based on Phase 2 trials is becoming more common. These medications typically have narrow indications and serve limited populations, making it difficult to conduct a sufficiently powered Phase 3 trial[15] – the standard evidence required by regulators. Patients with the serious conditions targeted by these drugs often have limited treatment options, with a rapidly closing window of time to change the course of their disease.

Decision makers are increasingly relying on Phase 2 data not just for drug approvals, but for determinations about public reimbursement. In such cases, health technology assessment (HTA) bodies may struggle to determine the value of the treatment, leading to greater reluctance to recommend it for listing. Indeed, oncology drug submissions based on Phase 2 trials are significantly less likely to receive a positive recommendation from CADTH, one of Canada's HTA agencies, than those backed by Phase 3 data.[10]

Even if a drug does ultimately receive a listing, the delay between regulatory Notice of Compliance (NOC) and public reimbursement leaves many Canadian patients in limbo for long stretches of time: an average of 580 days for oncology therapies and 670 days for orphan drugs.[14] These figures make Canada one of the slowest among OECD-20 countries to publicly reimburse innovative medicines, with a mean of 926 days from launch to listing, compared to the OECD-20 median of 519 days.[14]

Leading the charge

Why the gap? One reason: a lack of formalized early access pathways in Canada.[1] The UK, France, Germany, Italy, and Australia have established formal pathways for publicly funded early access, enabling patients to receive promising new therapies while decision makers gather the evidence required to make a final recommendation.[5]

An analysis of managed access in England between 2016 and 2022 determined that, of the 22 treatments (of which 20 for cancer) reevaluated following a period of managed access, 19 were recommended for routine use.[14] Most of the evidence submitted to resolve the uncertainty identified in the managed access agreement came from clinical trials, and some from real-world data (RWD). The researchers who conducted the analysis affirmed that "without managed access, these technologies would likely not have been recommended for routine use within the NHS in England."

Going even further, with the political will and the right systems in place, access delays can quite literally disappear. Four cancer drugs approved via Project Orbis,[16] a framework for concurrent regulatory review of oncology drugs

Without managed access, most of these innovative technologies would likely *not have been* recommended for routine use.

Authors of an ISPOR paper on managed access in England

developed by the FDA and adopted by partner countries, became available to UK patients on "day zero" – the very day the products were approved.[8] The early access agreements that made this possible sped up patient access to these four drugs by an estimated 200 days each – a crucial benefit for patients with aggressive cancers whose treatment options narrow every day.

Learning from leaders:
3 other countries with unique managed access experience[17]

COUNTRY	EXPERIENCE WITH MANAGED ACCESS AGREEMENTS
Spain	The Catalonia region has used results-linked reimbursement systems since 2011. In 2016, the region introduced a centralized system for implementing risksharing agreements between manufacturers and the CatSalut health service.
Italy	Managed access agreements (MAAs) are a standard feature of Italy's drug regulatory process. To evaluate drugs covered by such agreements, the Italian Medicines Agency relies on comprehensive and continuous collection of data, including real-world data from patient monitoring registries.
Israel	A third party (the MAA team) identifies health technologies most suitable for MAAs and then mediates negotiations between manufacturers and payers. After an MAA expires, the treatment will not be removed from the Israeli formulary, though the price may change.

National patchwork

The Canadian healthcare system, meanwhile, has no formal managed access policies or processes in place.[1] No doubt, having multiple public payers presents a challenge in this regard, and Canada does not benefit from the lockstep stakeholder alignment found in single-payer systems with established managed access frameworks. Instead, to date Canadian stakeholders have been managing early access needs on an informal, case-by-case basis.

One approach taken by Canadian stakeholders has been to propose innovative market access agreements that support timely access, notably OBAs. Precision oncology and rare disease medications have emerged as a natural fit for OBAs, due to their high costs, the niche populations they serve, and the urgency of the clinical need they address. Absent a formalized framework, however, concerns about administrative burden, infrastructure, and evidence requirements have exerted a drag on implementation.

At present, an estimated 10 to 20 "simple" OBAs exist in Canada, with payment models tied to outcomes such as disease progression scales used in clinical practice.[7] Canadian payers have confirmed that OBAs exist in the areas of oncology, hepatitis C, HIV, multiple sclerosis, ophthalmology, and cardiology,[8] but we're still just scratching the surface of feasible pan-Canadian solutions.

SETTING THE STAGE

At the same time, signs of forward movement are all around us. By all accounts, Canadian policymakers recognize the need for a consistent and equitable approach to early access, which requires government oversight and coordination between HTA bodies, the pCPA and payers. The year 2023 saw major movements in this space, with initiatives that manifest an openness to new approaches to support timely access for patients – including the makings of the first managed access pathway in Canada.

Early access leadership: three giant steps

To move the agenda forward, CADTH has implemented a new HTA process for time-limited recommendations (TLR) in September 2023, after stakeholder consultation earlier in the year.[4,31] The process applies to drugs that receive NOC with conditions (NOC/c) and sets the deadline for bridging evidence gaps at 3 years, after which new evidence must be provided for reassessment within 270 days. This framework makes it possible to issue a time-limited recommendation for therapies with immature but promising evidence, while enabling additional evidence to be generated and considered in CADTH's final recommendation. At present, CADTH regards only confirmatory Phase 3 clinical-trial data as suitable evidence to support reassessment and, while not accepting RWE as a matter of course, is open to considering it as supplementary.[32]

Building on CADTH's TLR process, the pan-Canadian Pharmaceutical Alliance (pCPA) has proposed a Temporary Access Process (pTAP) to inform listing agreements for medicines that follow CADTH's time-limited recommendation pathway.[5] pTAP lays the groundwork for manufacturers and public payers to establish an equitable, time-limited risk-sharing agreement to ensure the "sustainability and proper management of public funds in both the temporary funding period and beyond." If public funding does not continue beyond the temporary access period, the proposed process specifies that manufacturers would have to provide coverage "for any patient started on medication during the

We believe the introduction of *time-limited recommendations* is another way that health technology assessment can enable the timely and appropriate adoption of innovation and help governments expand access to treatments while managing uncertainty and risk.[31]

Suzanne McGurn, CADTH President and CEO

NEW CANADIAN PROCESSES TO ENABLE TIMELY ACCESS

1. **CADTH's** Procedures for Time-Limited Reimbursement Recommendations
2. **pCPA's** Temporary Access Process (pTAP)
3. **INESSS's** invitation to submit exploratory economic scenarios [French only]: Avis aux fabricants de médicaments, de dispositifs médicaux liés à l'administration de médicaments et de produits du système du sang

temporary period where for any reason public funding is not continued beyond the temporary period." A public engagement questionnaire on the process was open in August 2023, and updates are anticipated later this year.

In step with these efforts, in a June 2023 communiqué Quebec's HTA body INESSS invited pharmaceutical manufacturers to amplify their drug submissions with exploratory economic scenarios, which INESSS will include in advisories to the provincial health ministry.[6] Examples of such scenarios, which aim to optimize drug use and contain costs, include agreements to manage the budgetary impact of new medicines of uncertain value, agreements tied to performance, dose-ceiling agreements, and manufacturer-funded treatment initiation. "It's great to see that public institutions are open to modernizing the approval and listing process," says Eva Villalba, executive director of the Quebec Cancer Coalition, noting that "it will be important to include patients in these reforms to ensure they truly create value."

Getting real with real-world evidence

In fact, the whole managed access/OBA paradigm depends on the judicious use of RWE. As noted by Brad Millson, IQVIA Canada's General Manager, Real World Solutions, "RWE can play a pivotal role in informing managed access agreements by answering questions that cannot be done through traditional clinical trials in appropriate timeframes."

While 20Sense has already **reported on the progress of RWE earlier this year**, some developments that could impact the managed access/OBA paradigm are worth noting here. In May 2023, CADTH published a Guidance for Reporting Real-World Evidence, laying a foundation for the use of RWE in regulatory approval and HTA in Canada.[18] The document includes a detailed checklist to guide the submission of acceptable RWE. After the Guidance underwent a consultation process that drew 54 responses, CADTH published a feedback-response document described as "a crucial first step toward the end goal of integrating RWE into decision-making in Canada."[19] Next on the agenda: implementation procedures specifying how RWE will be appraised and used in decision making.

Quebec has also had its eye on RWE for many years now. As early as 2017, the 10-year Quebec Life Sciences Strategy proposed to establish an innovation fund to accelerate the adoption of new technologies and the use of RWE in research and elsewhere.[20] As a case in point, an INESSS lung cancer study used administrative clinical data to estimate the real-world outcomes of patients on a novel therapy called EGFR-TKI and compare the results to those reported in published studies.[21]

RWE can play a pivotal role in managed access by *answering questions* that cannot be done through traditional clinical trials in appropriate timeframes.

Brad Millson, General Manager, Real World Solutions, IQVIA Canada

MAKING IT HAPPEN

More than anything else, the managed access model requires buy-in from all stakeholders. The good news: if current activity is any indication, stakeholders are as eager as policymakers to get the ball rolling. The initiatives described below are paving the way to implementation.

Big-picture HTA

Managed access is making strides in British Columbia. An interactive session in the May 2023 CADTH Symposium, called Lifecycle Health Technology Assessment for Precision Oncology, reported on the progress toward a managed access infrastructure in the region, from data collection and use of RWE (including patient-reported outcomes) to managed access agreements.[22] The research challenged the evaluative process that constrains timely access and proposed a life-cycle approach to HTA[23] as an alternative. This big-picture model considers the value of a drug holistically, across all its phases. According to Dr. Tania Bubela, dean of Simon Fraser University's Faculty of Health Science, "implementation of life-cycle HTA has the potential to accelerate patient access to cost-effective new therapies."[30] The caveat: "The approach depends on ongoing monitoring of patient outcomes, which will require close coordination between regulators, payers, and systems."[30]

In line with this thinking, BC Cancer is piloting the life-cycle HTA framework within a program called PREDiCT [Precision Evidence Development in Cancer Treatment], co-funded by Roche Canada and the Canadian Personalized Healthcare Innovation Network. [22,29] The pilot's goal has been to apply the framework to a drug that has not undergone a complete HTA review and to use health-system data to generate RWE, while facilitating early access for patients. If the pilot phase proves successful, the PREDiCT framework will help shape new reimbursement pathways for personalized cancer treatments.[29]

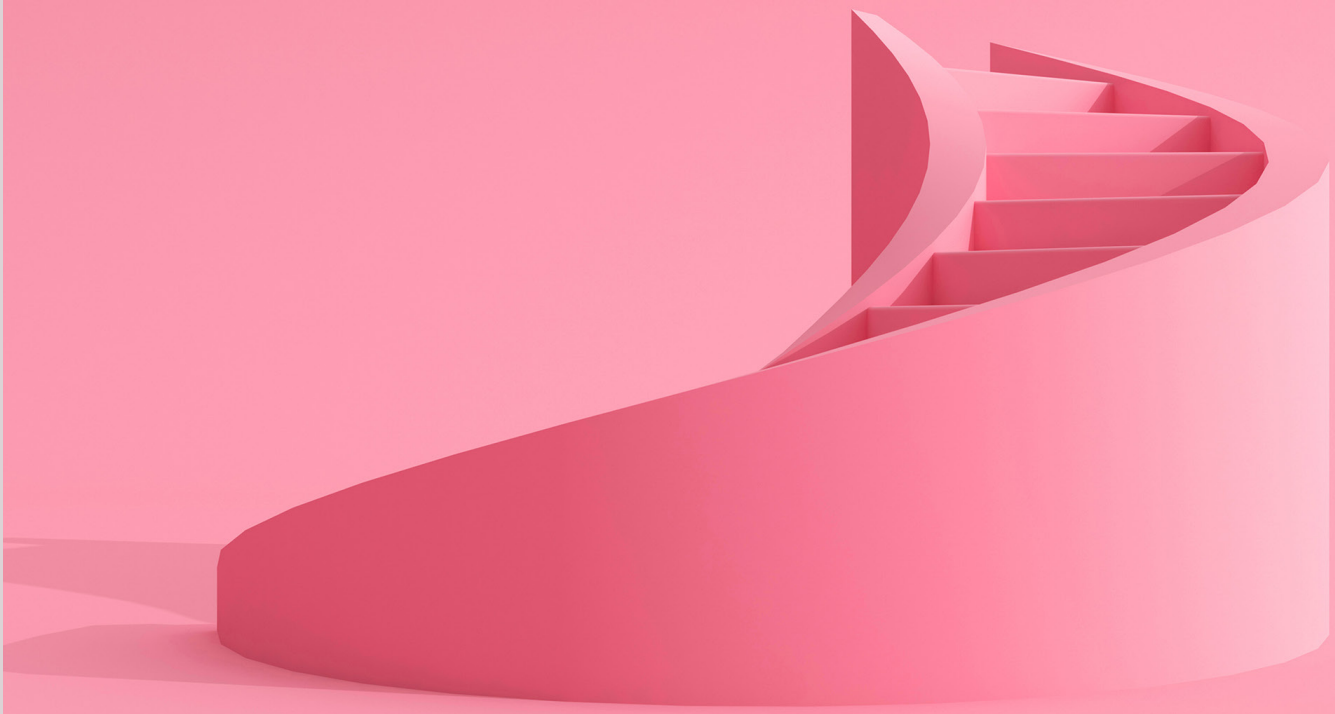
Better access on the Atlantic horizon

In addition to delivering value, new access pathways must save time. With this vision in mind, New Brunswick's Horizon Health Network has partnered with Amgen Canada to develop a new access pathway for innovative treatments that target a specific type of lung cancer.[24] The pathway runs parallel to the existing process for introducing new medications to market. Crucial to the scheme is that the province's Regional Health Authority will have direct access to therapy. Margaret Melanson, Horizon's interim president and CEO, notes that "the traditional pathway for bringing innovative medical solutions to market in Canada is very linear and can take two to three years from start to finish." The new access approach "is providing an express lane for patients to have access to new treatments."

OTHER INITIATIVES ON THE MUST-WATCH LIST

Here are four initiatives that promise to yield both information and action on the managed access and OBA front.

1. **The RWE and OBA Working Group,** a collective devoted to researching RWE and OBAs and removing implementation barriers for Canada, recently conducted research with public payers and drug manufacturers to gain insight into which OBA financial models are appropriate and preferred by Canadian stakeholders.[8] Stay tuned for the publication of the results.
2. In June 2023, **CADTH** announced upcoming changes to its reimbursement review process.[25] Intended to tighten all stages of the review process, these changes include streamlining review requirements for certain drug products, exploring how to incorporate new evidence midstream in a review, exploring innovative models such as OBAs, among others. The announcement also pledges to "bring greater transparency and clarity to our processes" and to "better engage with industry, clinicians, and patients with a view toward improvement." What's not to like?
3. **Montréal InVivo**, a nonprofit organization dedicated to fostering life science and health innovation in Quebec, has established a committee to explore value-based reimbursement agreements in the province.[26] The initiative will go through several phases, including identification of suitable therapeutic indications and uncertainties, characterization of the reimbursement agreements proposed for the selected treatments, RWE collection and analysis, and recommendations for guidelines and best practices. To Robin Durand, Montréal InVivo's Director of Innovations in Life Sciences, the project's greatest value lies in "the framework that we will develop and put into play to manage therapeutic uncertainty, using RWE to leverage better access to new science."
4. **The Government of Canada** has recently pledged to invest $1.5 billion over 3 years to implement its Rare Disease Drug Strategy, endorsed in 2019 to accelerate the diagnosis and treatment of rare diseases.[27] The vast majority of these funds ($1.4B) will be distributed to provinces and territories to improve access to new and emerging treatments, with the rest allocated to advancing research, evidence collection, and governance structures for rare diseases. Best case, the investment will lead to routine collection of RWE for rare-disease drugs and support eventual OBAs or other forms of managed access for these treatments. The devil will lie in the details, but the funds are an excellent start.



The project will identify a group of eligible patients in the first year, with the potential to expand in the future. John Snowden, Executive Director at Amgen Canada, applauds "the original thinkers at Horizon Health Network in New Brunswick who took on the challenge of navigating a complex system to put patients first. Echoing Ms. Melanson's comments, Mr. Snowden notes that "Canada's reimbursement review system is slow – delaying access by about 22 months after a medicine is approved by Health Canada. This new framework in New Brunswick will identify patients for treatment with a prescription medicine that targets a specific type of lung cancer that is metastatic or not amenable to curative therapy."

WHAT NEXT?

As these initiatives exemplify, managed access and OBAs have moved up the priority list for Canadian stakeholders. Other countries have shared their experiences with us, on the podium and in publications, and home-grown research has helped us understand how these tools might support innovation and best practices in this country.

Helen Stevenson, founder and CEO of the Reformulary Group and a leader in the specialty pharmaceutical space, frames the opportunity succinctly: "Every new specialty drug confronts us with three key questions," she says. "Does it work better than standard treatment? Does it not work as well as expected? Does it cost more?" Canadians need "good information so they understand that some drugs work better than others and there is usually more than one option to treat a condition."[28] Managed access and OBAs can give us the means to support access to the right treatments, collect data in the real world, and optimize outcomes for each patient.

While a step in the right direction, the initiatives described here will not necessarily streamline access to the extent patients require and deserve. We need not just progress, but commitment to setting and reaching access goals. As we move forward in the space, we must keep our focus on the central question: How can managed access approaches and OBAs be implemented to enable timely access for patients to novel therapies and ensure value for payers?

That's the crux of the matter: access and value. If a medication shows promise of value, patients should have access to it while we fill in the evidence gaps. Managed access schemes and innovative market access agreements such as OBAs make this possible. **Let's keep breaking down the barriers.**

Inspiration for Canada: Ensuring Access While Reducing Risk

Having lived and breathed managed access for much of his career, NICE's Thomas Strong is just the person to encourage Canada to explore such agreements

Thomas Strong is the Interim Associate Director for Managed Access at the National Institute for Health and Care Excellence (NICE), the UK's health technology assessment (HTA) agency. NICE helps facilitate optimal and timely care to patients, while ensuring value for the taxpayer. Thomas joined NICE in 2016, starting as a technical analyst and progressing to HTA adviser, a role that saw him develop managed access programs for cancer medications. His current position puts him at the helm of NICE's Managed Access Team, which is responsible for identifying candidates for managed access agreements (MAAs), delivering data collection agreements, and monitoring existing MAAs. In this conversation, Thomas shares his deep experience with MAAs and identifies key learnings that could help Canada move forward in the MAA space.

How do you define managed access and what is its rationale?

Managed access in the UK is a time-limited arrangement to give patients early access to promising new drugs. The process helps manage the uncertainty around evaluating a new treatment and ensures the NHS [National Health Service] is paying a cost-effective price during the managed access period. In truth, managed access is a compromise with reality: in an ideal world, we would routinely list all newly approved drugs. In the real world, where new therapies are sometimes approved on the basis of phase 2 trials or immature data, the evidence may be too uncertain for NICE to determine whether a new medicine is a good use of NHS resources. An MAA enables us to gather further evidence to make a final decision on cost-effectiveness, while also allowing patients to access potentially life-changing medicines by commercially sharing the risk with our industry partners.

What is the context for the establishment of MAAs in England?

In 2021, the UK spent over 17 billion pounds on health technology, of which a sizable proportion goes to cancer treatments, and there is a constant influx of cancer drugs coming down the pipeline. This means we have to balance two priorities: getting innovative drugs to patients as quickly as possible while ensuring value to taxpayers, who fund the NHS. We need to remember that, if NICE recommends a treatment that ends up not being cost-effective, it would be at the expense of other, higher-value treatments. Our two managed access funds – the Cancer Drugs Fund and more recently the Innovative Medicines Fund – grew out of these priorities. Together, these funds provide 680 million pounds per year to spend on innovative medicines and on expediting access to these drugs while managing risk.

What does "managing risk" look like?

It's important to be explicit about the risks to the different partners: the HTA body, the payer, but also industry and patients. For instance, in our original managed access process, treatments could be withdrawn from patients if NICE gave a negative recommendation. That risk was being borne by patients and it caused them a lot of anxiety. When we developed the Innovative Medicines Fund, we made it clear that the drug company, not the patient, would bear the risk by continuing to pay for treatments that were deemed to not be cost effective at exit.

How do you identify candidate drugs for an MAA, and how long does the process take?

In most cases, we enter into managed access because a promising drug is entering the market with immature data – but there can be other reasons, such as the clinical trials not being representative of NHS clinical practice. I should emphasize that MAA is only suitable for really promising new drugs. If we're worried that a drug may not work, managed access isn't the right vehicle for it. As for timelines, we seek to get from the decision-making committee to an MAA in about 35 days. It's an ambitious timeline that requires us to do a lot of work upstream and to monitor the entire pipeline.

How do you set drug pricing during the MAA period?

Drug prices are negotiated between NHS England and the company, with the parameters informed by the uncertainty and risk identified by NICE. In England we like to keep it simple, so we aim for a straightforward price discount during the MAA period. A discount is easy to transact and to negotiate. The key difference, compared to routine listing, is that this discount can apply to the specific indication that is entering managed access, rather than across all indications a medicine can be used for. Once the price is set, we enter the managed access period: patients get access, data is collected, and hopefully the evidence collected sufficiently resolves the uncertainty. At that point, as part of the commercial agreement process, a new price can be offered. If the data determines a drug to be more cost-effective than anticipated, industry has the opportunity to change the price to reflect that.

How long does the MAA period generally last?

We want to collect data as quickly as possible – within 5 years is our limit. We don't want to keep treatments suspended in managed access forever. We have had some drugs move through a MAA in as little as 6 months, while others have pushed right up against our 5-year limit. Our median has been 3 years.

Has the effort to establish MAAs been worthwhile? Have these agreements fulfilled their intended benefits?

We have seen 55 cancer drugs come through the MAA process, and 28 of them have exited from managed access – in most cases proceeding to routine listing. In some cases, the data resolves the uncertainty, but reveals that the medication is not as cost-effective as the drug company expected. This doesn't mean the process wasn't a success. On the contrary: it affords a renegotiation point to enable a transition to routine listing.

NICE and the NHS have recently established some "Day Zero" early access agreements. Is this a goal for NICE, and how did you make that happen?

With a Day Zero agreement, a product is listed on the day it receives regulatory approval. It is definitely a goal. NICE has designed its methods and processes to align with the regulator, which means doing a lot of work upstream. To do this, we need a framework for streamlined entry, which means coordinating with other policymakers. Managed access doesn't occur in a vacuum: a lot of other policy developments must fall into place to make it possible. For example, we have the Early Access to Medicines Scheme, whose purpose isn't about value: it's about unmet need and access, and it happens before NICE evaluation.

Managed access is only suitable for really promising new drugs. It allows us to balance two priorities: getting innovative drugs to patients as quickly *as possible while ensuring value* for taxpayers.

Managed access doesn't occur in a vacuum: a lot of other policy developments must fall into place to make it possible.

What role does real-world evidence [RWE] play with MAAs?

To date, ongoing clinical trials have been the key driver for resolving uncertainty, rather than RWE. Why would this be? Let's say we already have 5 years of data from a clinical trial, with 3 more years to go. In such a case, the RWE will never catch up to the data from the ongoing trial. That said, RWE is being used with increasing frequency and is often the only source of evidence to resolve uncertainty for rare-disease drugs. Indeed, some rare-disease drugs have had such good results at phase 2 that clinicians consider it unethical to delay access by requiring Phase 3 trials. In such a case, RWE fills the evidence gap during a managed access period.

What are some best practices for generating RWE?

Focus on the data that matters most. With RWE, it's tempting to try and collect everything. This has a real risk attached to it – namely, that you don't actually collect the data that would make a difference to decision-making. Also, there is a real and often underestimated burden attached to collecting, analyzing and using real-world data.

Once the evidence is generated, how does NICE manage the reassessment of the drug within the MAA?

With innovative medicines continually being introduced, we recognize that the landscape may change. We need to look at the totality of the evidence and make decisions that are relevant for people now, not validate a decision that is several years out of date using just the evidence collected within managed access. That's why it's critical for NICE to be involved at both the front end and exit of MAAs, because we want to make sure we have cost-effective medicines in the NHS at all points in time.

How do you ensure a smooth exit from MAAs?

Above all, you need to be clear on what the exit process will look like. Predictability is key for all stakeholders, and you don't want to be changing things all the time. If you don't set up clear expectations, you're not giving industry the best opportunity to prepare effectively. You also want the exit to be as streamlined as possible, which means you need to work backwards to understand how you're going to transition into routine listing.

What role should industry play in MAAs?

We engage upstream, so we start talking to companies in advance of an anticipated MAA. During the managed access period, we involve and regularly meet with patients and clinicians, and possibly other stakeholders such as registries and industry, to ensure we are proceeding according to plan and collecting the data needed to resolve the uncertainty. When RWE is involved, we often need to course-correct during the evidence generation period. Regular touchpoints with industry can help us ensure the RWE is fit for purpose and will support a treatment's value proposition, which enables us to successfully exit the MAA period.

What tangible next steps would you recommend for us here in Canada, to help ensure timely access to novel therapies with uncertainties?

Identify drugs that may be suitable for a MAA early on, so you can get the process rolling in a timely manner. Aim to streamline and standardize the entry and exit process for MAAs to set clear expectations for all stakeholders. And keep exploring the potential for RWE to resolve uncertainties. The advantage of RWE, compared to clinical trials, that it reflects the realities of actual use within a health system. But it's a double-edged sword: RWE can be messy and complex to analyze. Keeping it as simple as possible reduces your risk. Just because we have very complex new medicines doesn't mean we can't have simple solutions.

The exit process for MAAs needs to be clear. *If clear expectations are set*, we are giving industry the best opportunity to prepare effectively.

On the reading *list*

Early access for innovative oncology medicines: a different story in each nation

What goes in must come out: an analysis of NICE recommendations for drugs exiting managed (early) access in England

Outcomes-based agreements: Why do they matter for the future of healthcare systems?

CADTH's Time-Limited Recommendation Category Aims to Support Earlier Access to Promising Drugs

Opinion: Precision medicine offers cancer patients a better chance at survival – why are we making them wait?

New drug to treat prostate cancer may be out of reach for most Canadians

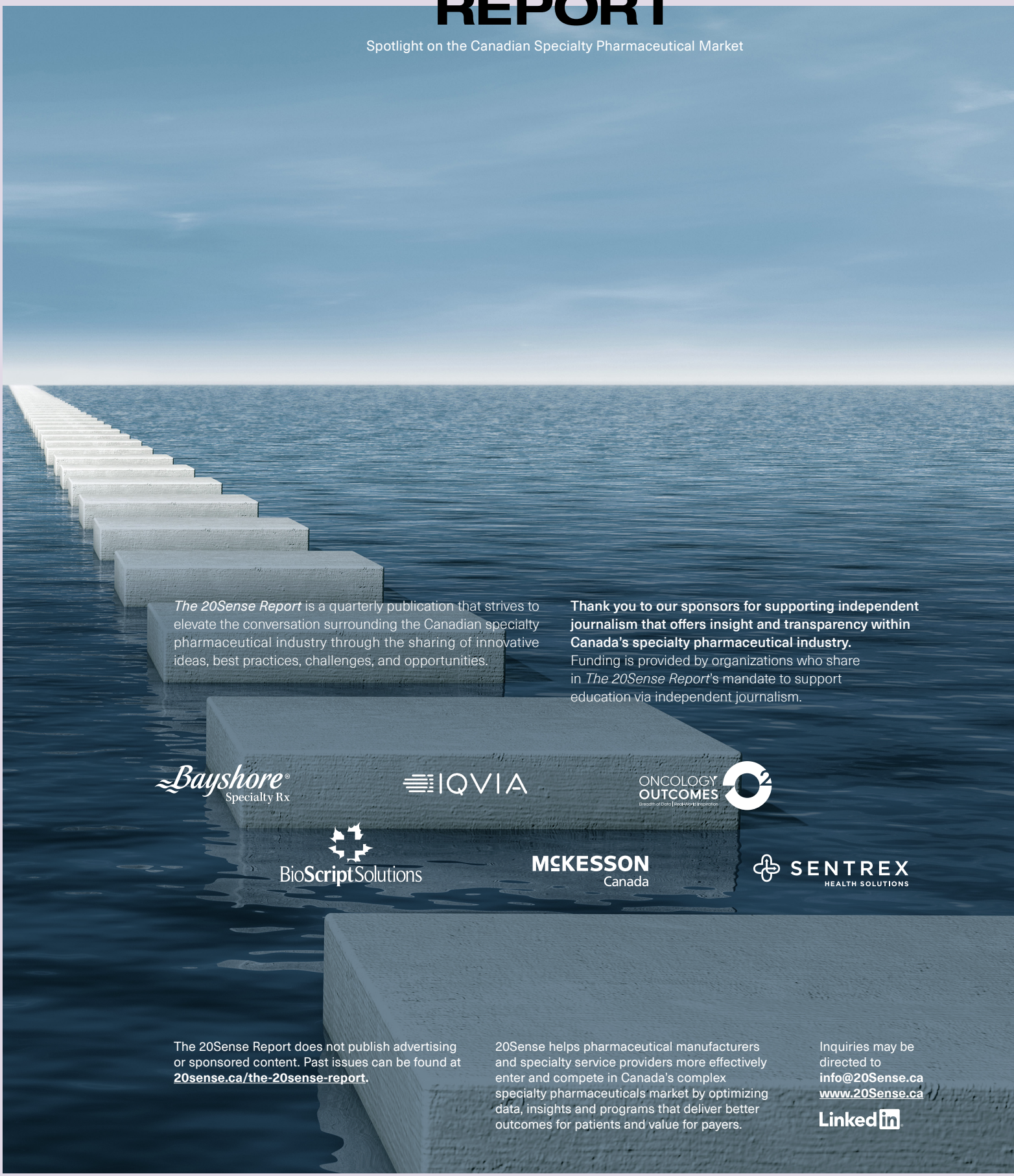
References

1. Cowling T et al. Early access for innovative oncology medicines: a different story in each nation. J Med Econ 2023;26:944.
2. Cheung WY et al. Building infrastructure for outcomes-based agreements in Canada: can administrative health data be used to support an outcomes-based agreement in oncology? Supportive Care in Cancer 2023;31. **https://tinyurl.com/bdf987n4**
3. The 20Sense Report. Issue 16, April 2021. **https://tinyurl.com/5n8tvwpb**
4. Proposed Process for Time-limited Reimbursement Recommendations. CADTH. March 2023. **https://tinyurl.com/yf3aejww**
5. pCPA temporary access process (pTAP). pCPA 2023. **https://tinyurl.com/57y5sybn**
6. Avis aux fabricants de médicaments , de dispositifs médicaux liés à l 'administration de médicaments et de produits du système du sang. INESSS. June 12, 2023. **https://tinyurl.com/2evy5v2r**
7. Canadian Outcomes Based Agreements Experience and Perceptions: Survey Results, RWE & OBA Working Group, October 2021.
8. 20Sense original research.
9. Hoskyn SL. Explaining public reimbursement delays for new medicines for Canadian patients. Innovative medicines Canada. **https://tinyurl.com/3wy29r5m**
10. Li YYR et al. Reimbursement recommendations for cancer drugs supported by phase II evidence in Canada. Curr Oncol 2020;27:e495.
11. Clinical development success rates and contributing factors 2011-2020. Biotechnology Innovation Organization. **https://tinyurl.com/mprrpu9h**
12. Meds Pipeline Monitor 2022. Government of Canada. Last modified June 27, 2023. **https://tinyurl.com/cxpwc9ye**
13. Early access to innovative medicines. Medlior Health Outcomes Research Inc. CORD conference presentation, March 2023.
14. Bee C et al. What goes in must come out: an analysis of NICE recommendations for drugs exiting managed (early) access in England. NICE poster. [Full article in Value in Health 2022;25:S478.]
15. Dubuc A. Cancer treatment: Canadians don't have access they expect and deserve, Oncology Medicine Access Roundtable. April 2022.
16. Project Orbis. FDA Oncology Center of Excellence. **https://tinyurl.com/5vsdymf**
17. McPhail M et al. Should Canada adopt managed access agreements in Canada for expensive drugs? J Law Biosci 2023;10:1.
18. Guidance for reporting real-world evidence. CADTH. May 2023. **https://tinyurl.com/mr3h49dn**
19. Guidance for reporting real-world evidence: response to stakeholder feedback. CADTH. May 2023. **https://tinyurl.com/7m9xw63u**
20. 2017-2027 Quebec Life Sciences Strategy. Government of Quebec. 2017. **https://tinyurl.com/yjabws43**
21. Utilisation en contexte québécois des inhibiteurs de la tyrosine kinase du récepteur du facteur de croissance épidermique (EGFR) pour le traitement du cancer du poumon. Coup D'Oeil. INESSS. **https://tinyurl.com/ykuv4bu2**
22. CADTH 2023 symposium. Preliminary program. **https://tinyurl.com/2jt6wu2z**
23. Regier DA et al. A perspective on life-cycle health technology assessment and real-world evidence for precision oncology in Canada. NPJ Precis Oncol 2022;6:76.
24. Innovative partnership will deliver expedited access to cancer treatment for New Brunswick patients. Horizon Health Network. June 6, 2023. **https://tinyurl.com/2utz68r8**
25. Upcoming improvements to the CADTH reimbursement review process. CADTH. June 5, 2023. **https://tinyurl.com/3fy7ax2p**
26. Projet sur les ententes basées sur la valeur. Montreal INVIVO presentation. July 6, 2023.
27. Government of Canada improves access to affordable and effective drugs for rare diseases. Health Canada. March 22, 2023. **https://tinyurl.com/2huke6cu**
28. Technology and healthcare walk hand-in-hand to provide accessibility, with Helen Stevenson. The Brand Is Female podcast. August 22, 2023. **https://tinyurl.com/4ba68ufy**
29. Roche Canada Announces Collaboration to Improve Access to Personalized Healthcare with Real World Evidence. BC Cancer. May 28, 2021. **https://tinyurl.com/3a6x5ebj**
30. Life cycle health technology assessment: real-world evidence for precision oncology. Genome BC. November 23, 2022. **https://tinyurl.com/4w76erpw**
31. CADTH's Time-Limited Recommendation Category Aims to Support Earlier Access to Promising Drugs. CADTH. September 2023. **https://tinyurl.com/2bkjadjj**
32. CADTH Procedures for Time-Limited Reimbursement Recommendations. CADTH. September 2023. **https://tinyurl.com/53tpjbhe**

20 SENSE

THE 20SENSE REPORT

Spotlight on the Canadian Specialty Pharmaceutical Market



The 20Sense Report is a quarterly publication that strives to elevate the conversation surrounding the Canadian specialty pharmaceutical industry through the sharing of innovative ideas, best practices, challenges, and opportunities.

Thank you to our sponsors for supporting independent journalism that offers insight and transparency within Canada's specialty pharmaceutical industry. Funding is provided by organizations who share in *The 20Sense Report*'s mandate to support education via independent journalism.

Bayshore Specialty Rx

IQVIA

ONCOLOGY OUTCOMES

BioScript Solutions

McKESSON Canada

SENTREX HEALTH SOLUTIONS

The 20Sense Report does not publish advertising or sponsored content. Past issues can be found at **20sense.ca/the-20sense-report**.

20Sense helps pharmaceutical manufacturers and specialty service providers more effectively enter and compete in Canada's complex specialty pharmaceuticals market by optimizing data, insights and programs that deliver better outcomes for patients and value for payers.

Inquiries may be directed to
info@20Sense.ca
www.20Sense.ca

LinkedIn