Innovative Agreements Framework

INNOVATIVE MEDICINES CANADA

MÉDICAMENTS NOVATEURS CANADA

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Executive Summary

- Many new treatments and innovative medicines coming to market (e.g. curative treatments, gene therapy, specialized medicines, rare disease drugs) are not well served by the traditional negotiation approach that relies on setting prices or capping expenditure based on anticipated volumes or estimated cost-effectiveness. If public drug plan payors and manufacturers cannot agree to broaden the range of negotiated agreement types beyond the traditional agreements, Canadians who depend on Canadian drug benefit plans will have increasing difficulty accessing novel treatments for their conditions or diseases.
- Public payors and manufacturers can collaboratively develop a pan-Canadian process that includes different approaches beyond simple price first dollar discounts and volume agreements. This new process will help patients benefit from timely access to new treatments while providing increased value and improved fiscal sustainability for payors.
- Other nations have implemented innovative agreements to address the challenges of some products with significant success. This document identifies examples of innovative agreements developed and used by public jurisdictions outside of Canada. It also describes the high-level characteristics of these types of agreements.
- To achieve an innovative agreements framework, a senior-level commitment from jurisdictions within the pan-Canadian Pharmaceutical Alliance (pCPA) along with the empowered participation of senior leaders from both industry and governments is essential.
- The innovative pharmaceutical industry proposes establishing a working group with a mission and mandate to create an innovative agreements framework.
- This document was prepared to initiate the discussion with the pCPA Governing Council to explore the merits of jointly developing and implementing an innovative agreements framework. (See Fig. 1.) This paper is intended not to be comprehensive but rather to articulate some of the opportunities and challenges facing both payors and manufacturers as well as to provide some examples of the following types of agreement options:
    - Performance-based;
    - Amortization;
    - Subscription;
    - Package; and
    - Portfolio.

Introduction

In recent years, an increasing number of innovative, high-impact treatments have come to the market, bringing with them the opportunity to benefit patients and improve the sustainability of the healthcare system through introducing significant savings to other parts of the healthcare system by reducing and even eliminating expensive and traditional healthcare interventions, including lengthy and repeated hospital stays. This trend is expected to increase in the near future. As an example, according to the *Medicines in Development for Cell and Gene Therapy 2020* report from the Pharmaceutical Research and Manufacturers of America, over 100 diseases and conditions are being explored for potential treatment with cell and gene therapies, and 362 cell and gene therapies are in development. Currently, there is no framework in place to adequately address the challenges these types of important therapies will have on our healthcare system.

Manufacturers are committed to bringing these innovations to market, and patients, clinicians and governments want timely and flexible access to these treatments with an efficient lifecycle approach. However, the current public structures, budget management, and accountability mechanisms have struggled to adapt to these advancements. For example, a small but growing number of innovative treatments are not equitably available across all provincial, territorial and federal drug programs in Canada. Additionally, for a growing number of treatments, the specific diagnostic test required prior to initiating therapy is not readily available. It is also problematic that some treatments managed by government drug processes require products, services and administrative processes outside the control of drug plan managers.

Since its inception in 2010, the pan-Canadian Pharmaceutical Alliance (pCPA) has been mandated "to achieve greater value for publicly-funded programs and patients through the use of the combined negotiating power of participating jurisdictions."[1] Over the past 10 years, most agreements have set prices based on anticipated volumes and cost-effectiveness. In many cases, the price and volume agreements have been a reasonable and effective way to achieve value for the drug plans and access for patients. However, it is increasingly clear that a broader range of agreement types needs to be formally incorporated into the inventory of agreement types to be negotiated.

[1] The Council of the Federation, Canada's Premiers, "The pan-Canadian Pharmaceutical Alliance, "https://www.canadaspremiers.ca/pan-canadian-pharmaceutical-alliance-archives/."

Current negotiation practices are too limited in their capacity to address certain products, particularly products that have limited or uncertain clinical and cost-effectiveness data, that have significant upfront costs, that require access to health system resources outside the responsibility of provincial drug benefit plans, that challenge budget certainty, and that require innovative diagnostic technologies to inform a patient's treatment candidacy. In addition, the rigidity of the current reimbursement pathway — from regulatory approval to the product listing agreement (PLA) stage — can cause delays and present a barrier to optimizing the process based on the needs of patients, the healthcare system and society. As a result, patients who would benefit from treatments cannot access them, clinicians are constrained by not being able to offer the most appropriate available care, and governments face increasing dissatisfaction with the quality of their health system. This new reality has resulted in both industry and pCPA acknowledging the need to expand the negotiation toolbox by considering the use of innovative agreements.

Several different types of innovative agreements are being used with growing frequency in other jurisdictions. Given the rising complexity of innovative treatments seeking entry to the Canadian market, there is the potential to adapt these types of agreements and combine their features to address specific issues and concerns identified. With an open-minded approach to problem-solving that is flexible, agile and fit-for-purpose, manufacturers and payors can consider changes not only to the agreement types but also to the regulatory, legislative and IT infrastructure that supports the new system.

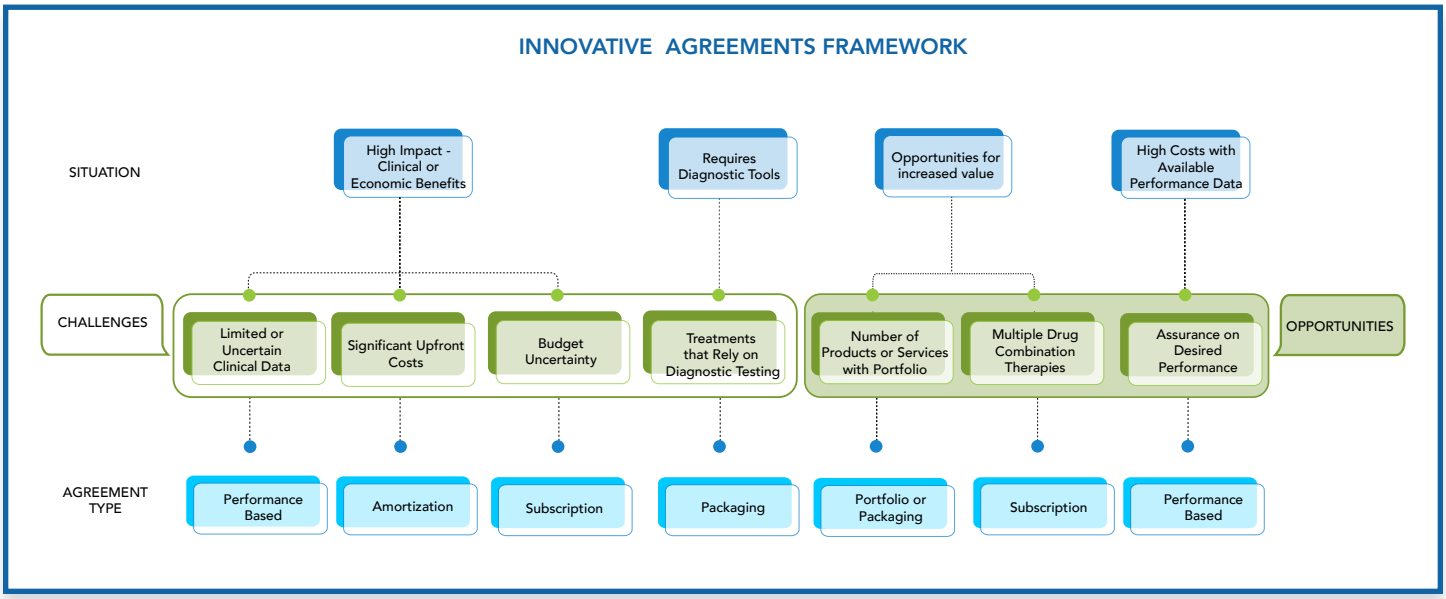
The innovative pharmaceutical industry has formed a working group to develop an innovative agreement framework to be used in public negotiations. The working group seeks to achieve the following goals:

- Develop a draft framework to articulate the merits of several different innovative agreements that could be used with Canadian public payors.
- Present the draft framework to the membership of Innovative Medicines Canada and BIOTECanada, through their respective processes, in order to seek their input and support.
- Present a final draft framework to the pCPA Governing Council and have a robust conversation with its members about the issues and merits of adopting such a framework, subject to any modifications as agreed to by both parties.
- Seek final approval from Innovative Medicines Canada, BIOTECanada and the pCPA Governing Council, and have the framework adopted and implemented as part of the pCPA Brand Process Guidelines.

Framework

Categories are not mutually exclusive, but the types of agreements are classified below based on their primary intent.

Figure 1. Innovative Agreements Framework



Challenges

Limited or uncertain clinical data

Limited or uncertain clinical data can occur in a variety of trial situations, including:

- In rare diseases and conditions;
- In small patient populations;
- When the study or comparator populations may not represent the Canadian population;
- When there is a novel or targeted biomarker;
- When a novel, unconventional, non-randomized or non-comparative clinical trial design needs to be used or changed for pragmatic and ethical reasons (e.g., Phase 2, single-arm umbrella, basket trials); and
- When high unmet need justifies an expedited regulatory pathway, even though long-term follow-up data is lacking.

Clinical trials in such situations are often conducted for a much narrower patient population than the broader population that could benefit; for rare diseases, the sample size can be incredibly small. This can result in clinical uncertainty, especially as it relates to the translation of results into clinical practice and comparing clinical value with that of alternative therapies.

In addition, regulatory conditional approval requirements may not align with health technology assessment (HTA) and payor requirements. For rare diseases, furnishing additional data required by an HTA or a payor within a trial setting may be infeasible or impossible.

In the situations listed above, there can also be a lack of natural history data to characterize patients with the disease or a lack of biomarkers to provide a baseline on prognosis for those who go untreated or with standard-of-care therapies. This can lead to a lack of contextual evidence to characterize the clinical value of the drug in question.

Finally, such situations can also lead to uncertainty in comparative cost-effectiveness, especially due to a lack of a comparator arm and long-term follow-up.

Significant upfront cost

In some situations, significant upfront costs are required for high-impact products. These products can have certain clinical efficacy, be deemed "cost-effective" by HTA organizations, or have a relatively accurate measurement of budget impact. Costs may be particularly high when a cure is launched to treat a disease with a high prevalence population or when the cost to set up treatment is expensive. In these situations, affordability for payors becomes challenging due to the significant budget impact from a cost that must be paid at once. From a manufacturer perspective, the volume of patients on therapy may not continue over time, and so there needs to be recognition for bringing such an innovation to the market.

Budget uncertainty

Budget uncertainty can arise due to factors such as the following:

- Sufficient information about the incidence or prevalence of the condition is not available due to a lack of surveillance and analytical resources and/or diagnostic precision to identify specific types of patients.
- Many treatments may be available, but the new product could become the new standard of care and thereby displace other treatments.

- The expected clinical benefit in the real world is significantly different than what was observed in the clinical trial or the ability to effectively diagnose the condition may be significantly different than expected.
- There could be a large patient population outside of the narrow clinical trial eligibility criteria.

Budget uncertainty is very common for drugs that are the first to treat certain indications. For many drugs that are the first in a medical therapy or group of therapies to treat an indication, it is difficult to accurately predict the budget impact because often when there are no medical therapies, diagnoses are seldom made and tracked in a manner that is accurate or accessible for analyses.

Examples

Nonalcoholic fatty liver disease (NAFLD) and resulting nonalcoholic steatohepatitis (NASH) are highly prevalent in the United States. NASH has been recognized as a significant form of chronic liver disease, a common cause of cirrhosis and hepatocellular carcinoma and, increasingly, an indicator for liver transplantation, resulting in a considerable financial burden on healthcare resources. NASH is increasingly seen as a cause of end-stage liver disease and is currently the second most common etiology of hepatocellular carcinoma (HCC) requiring liver transplantation. Increasing age, obesity, and type 2 diabetes mellitus have been consistently identified as risk factors for fibrotic progression to cirrhosis. Existing literature on the epidemiology of NAFLD is made complicated by varying case definitions, methods for assessment, small and heterogeneous populations, and variable analytic approaches. In the United States, there are currently no approved drugs to treat NASH.[2] For future therapies entering a completely new treatment landscape that is faced with challenging epidemiology data, this creates a large degree of budget impact uncertainty.

Alzheimer's disease is another therapeutic area with a high degree of budget uncertainty. Therapies for Alzheimer's disease pose a challenge in that costs and benefits accrue over a longer period, impact different budgetary siloes and require data to support decreased reliance on caregivers and other health and public health system resources that are challenging to measure.

[2] Chris Estes and others, "Modeling the epidemic of nonalcoholic fatty liver disease demonstrates an exponential increase in burden of disease," *Heptalology* 67, no. 1 (January 2018): 123–133.

Treatments that rely on diagnostic testing

As precision medicines continue to enter the Canadian market, an increasing number of innovative technologies are critical to ensuring not only that the right patient receives the right treatment but also that the treatment is achieving the desired clinical benefit. Increasingly sophisticated diagnostic testing (such as comprehensive genomic profiling to identify cancer biomarkers) improves the precision with which clinicians can determine the most effective treatment. However, just as these new and effective treatments are entering the market, numerous market access challenges have arisen.

Example

Radiopharmaceuticals are being developed to provide precise diagnoses. However, their very nature creates challenges around physician fee schedules, hospital and ambulatory diagnostic imaging procurement and access to the clinicians needed to interpret these tests. To ensure the most appropriate candidate is chosen for a treatment, the demand for diagnostic tools, such as positron emission tomography (PET) units, is expected to increase. At present, there are fewer than 60 PET units in Canada, and they are all used, with some rare exceptions, only for oncology. We expect demand to increase rapidly for access to PET for such conditions as Alzheimer's and other neurological disorders to determine if a novel treatment is the best course of care. Substantial investment is needed to increase the number and the types of services PET devices are to be used for, and to increase the availability of PET tests when they are a precondition in order to ensure patients will have access to the treatment.

In addition, the processes to determine an insured physician funding mechanism (e.g., fee-for-service or alternative payment plan) are managed in a very different way than drug budgets.

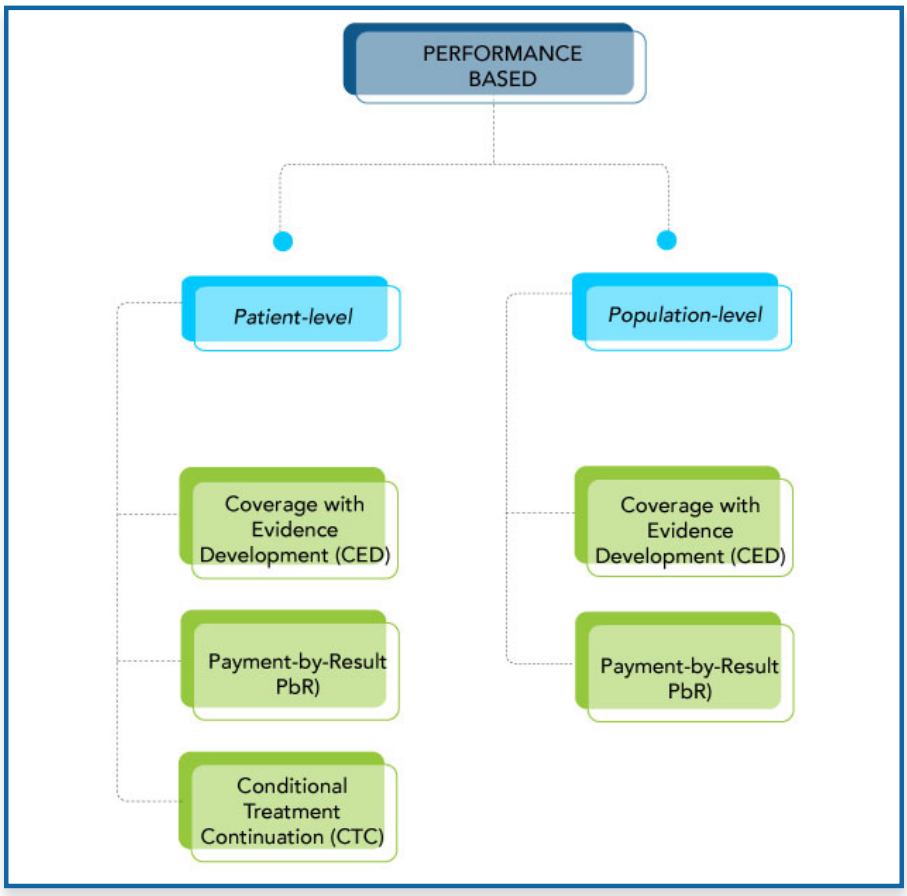
These challenges fall outside the pCPA and often involve multiple companies, some of which are not pharmaceutical companies. The traditional silo-based budget management processes within the health system, along with different and often uncoordinated evaluation and reimbursement pathways, also present a challenge.

Types of agreements

Performance-based agreement model

Performance-based agreements track the "performance" of a drug in a defined patient population over a specified period of time to determine if the agreed-to clinical benefit has been achieved or maintained. In some cases, the agreement reimburses the manufacturer only for those patients who have achieved the benefit. Other agreements provide for gradients of success, where a percent of the product's cost is reimbursed, should there be partial benefit or performance. Through this type of agreement, the drug plan is afforded an element of risk protection by reimbursing the drug only when designated benefits have been attained.

Figure 2. Performance-based agreement[3]



[3] Adapted from M. Wenzl and S. Chapman, "Performance-based managed entry agreements for new medicines in OECD countries and EU member states: How they work and possible improvements going forward", OECD Health Working Papers, No. 115, OECD Publishing, Paris, 2019, https://doi.org/10.1787/6e5e4c0f-en.

Benefits

Performance-based agreements are often used to facilitate access to promising drugs with significant clinical or pharmacoeconomic uncertainty. They can also be used in many other situations as a means of ensuring that "value" — as described by an agreed-upon performance metric — is obtained. These agreements can also provide more assurance that only those patients most likely to benefit from the innovation are the intended market.

The benefit of a performance-based agreement is that a product can secure formulary access that payors may have otherwise hesitated to reimburse pending additional evidence. As benefits are achieved over time, it is also possible that payors may become more comfortable with making the product an eligible benefit for more patients.

Performance-based agreements are increasingly being viewed as part of an essential toolkit for value-based healthcare funding in many other countries.

Potential uses

Performance-based agreements for drugs with uncertain clinical or pharmacoeconomic evidence can pave the path to a long-term, permanent solution of risk-sharing. They can expedite access to promising medications and influence funding status based on the analyses of real-world evidence.

- **Coverage with evidence development:** Under this type of agreement, conditional patient access and reimbursement is provided for therapies for diseases with high mortality or morbidity, where the length of follow-up time for clinical trials is limited. There is agreement to reassess outcomes, criteria, listing status, etc., when either clinical trial or real-world long-term follow-up data become available. Cost-effectiveness analysis is updated as longer-term data becomes available, to reassess value and pricing considerations.
- **Risk-sharing based on response to treatment:** Outcomes routinely collected in clinical care are used as the basis of treatment renewal (e.g., objective imaging response in oncology post-treatment initiation). This data could be collected in various forms (patient support programs, registries, special authorization forms, etc.), requiring various levels of infrastructure development for support.
- **Performance-based agreement at patient level:** Payors get up to a 100% rebate if a patient stops taking the drug before the drug has time to produce clinical outcomes. For simplicity, administrative drug claims databases can be used.

- **Performance-based agreement at population level:** Payors get a percentage rebate that is tied to aggregate adherence data instead of volume. In these cases, a higher rebate could be issued if lower adherence is detected based on refill timelines.
- **Economic or utilization performance-based agreement:** Payors get a percentage rebate that is tied to the increase in number of patients switching from a more expensive, clinically equivalent alternative. This can be determined through data from public drug programs.

At one level, these types of agreements directly link to a patient's health performance. However, methods for the required data collection, analysis and management need to be explored collaboratively with government. Administrative data can be used as a proxy in patient-level, population-level and economic or utilization performance-based agreements. For some products and conditions, there will be a desire to follow the clinical journey of patients over time, perhaps years, something that requires significant discussion and agreement. These types of agreements necessitate a reorientation from inputs (dollars spent) towards paying for patient outcomes, which should be the desired intent of a public healthcare system.

Considerations

The complexity of performance-based agreements and the time and resources they require from governments, healthcare professionals, manufacturers and patients pose significant challenges for their implementation. Applying these types of agreements appropriately and sharing in their successes and failures could significantly improve access to complex new treatments. Most importantly, payors and manufacturers must align on goals and objectives for performance-based agreements. Performance-based agreements are not appropriate in all cases, and there should be transparent and collaborative discussions around where additional resources required for these types of agreements are justified.

1. Substantial administrative burden and cost are associated with performance-based agreements, and many European Union countries have questioned their benefits, particularly whether these agreements are achieving payor objectives. Therefore, an official framework must be applied in early discussions to identify which products are suitable candidates for performance-based agreements and to provide clarity on how risk will be shared, what metrics to track, and what "challenge" the agreement will solve.

2. Currently, data infrastructure, data ownership and timely access to existing data are barriers to implementing more performance-based agreements. The lack of comprehensive, national, real-world-evidence data sources makes data integration difficult and leads to a limited capacity to capture accurate outcomes. Where data is limited, outcome tracking can be improved through:

- Patient program data and consent
- Third parties to capture real world data, build infrastructure, insure and adjudicate
- Provinces that have the ability to track data as proxies
- Existing national networks of clinical practitioners

3. The current "one and done" decision-making mode must evolve into a lifecycle approach to help all stakeholders take on appropriate risks in a timely way to optimize patient impact and to refine or adjust the approach as needed. Performance-based agreements require establishing ongoing monitoring and measuring processes to ensure that all parties have confidence in the agreement and that capacity is built to support more of these types of arrangements cost-effectively.

4. It goes without saying that compliance and legal issues must be considered prior to providing a performance-based approach.

Amortization agreement model

The amortization model (sometimes referred to as an annuity payment) refers to an agreement in which lump-sum payments or a series of payments are made over a specified time period.

Benefits

The following are some of the benefits of an amortization approach:

- **Budget "shock absorption":** There are circumstances where a new innovation comes onto the market and the benefit is so compelling that it would be unreasonable not to make the product available. However, it may not be feasible to fund the demand within an annual budget cycle. This was one of the major dilemmas faced by both payors and manufacturers when the new treatments for Hepatitis C entered the market. Having an amortization model in place allows for the "smoothing" of expenditures over time, thereby spreading the budget pressures over a number of years, rather than one or two years.

- **Budget "warranty protection":** There may be circumstances where although the evidence suggests the treatment is curative, questions remain about the confidence in the product's cure-rate, especially for the years after the treatment is provided. Accepting a treatment as curative can be viewed as a risk for payors, especially if the treatment cost per case is high and/or the number of people being treated is large. A budget management tool such as an amortization agreement builds in time to reasonably satisfy both patients and payors that the product has achieved the desired

results. Payors can agree to spread payments over the number of years determined to be the functional "cure" time. If, for some reason, the disease recurs within the "warranty" period (i.e., length of the agreement), then the payor ceases payment.

Potential uses

The amortization model could be applied in the following situations:

- Curative medicine and/or gene therapy for a rare condition with a well-defined patient population, where there is an unusually large untreated population of patients.
- Curative medicine and/or gene therapy for a rare condition with a well-defined patient population.
- Curative medicine and/or gene therapy for a rare condition where there are questions as to the potential size of the patient population.
- In situations where there is an expected high number of patients at launch and the impact to the budget is high very quickly.

Considerations

Manufacturers and governments should note the following when considering the amortization model:

1. **Accrual budget management:** The amortization model can present challenges for the drug plan and cross-ministry budgeting and accountability.
2. **New program design:** New programs may need to be designed specifically to address products, services and patients where access would not be provided, based on existing programs.
3. **Alignment of coverage:** To determine the implications of an amortization model, the market characteristics of the drug coverage for rare diseases need to be reviewed. Are patient characteristics similar across both the public and private coverage populations? How is coverage impacted when a patient moves from one jurisdiction to another or from public to private (or vice versa)? Are the number of drugs, especially for rare and ultra-rare diseases, similarly available for both public beneficiaries and private drug plans? Governments and manufacturers need to consider the merits of ensuring consistency of coverage over time and reducing patient off-loading from private to public payors.

4. **Duration of agreement:** How long is a reasonable time period for a multi-year payment arrangement? It may be difficult to follow up with patients to administer multi-year payments.
5. **Evolution of treatments:** How does the payor address significant changes in treatment alternatives?
6. **Sole-source contracting:** Some amortization models may be considered to be sole-source contracts unless they are part of a formal service delivery program. At present, most governments either disallow sole-source contracts or limit their usage to lower value financial commitments.
7. **Failure to supply:** In cases where there is a disruption in supply during the amortization period, considerations need to be taken into account on how to address for this.
8. Compliance and legal issues must be considered prior to providing an amortization approach.

Subscription agreement model

A subscription model refers to an agreement in which payors pay a set amount for unlimited patient access to a specific product or products over a period of time.

Benefits

The following are some of the benefits of adopting a subscription model for certain therapies:

- **Budget certainty:** Fixed payments offer certainty that can reduces risk to both parties. Manufacturers are guaranteed a negotiated level of revenue while payor spending is capped.
- **Broad access:** The subscription approach may allow payors to offer broad access across different public plans, and beneficiaries while securing substantial cost savings.
- **Appropriateness:** A subscription agreement offers the flexibility to provide treatment for those who need it, rather than creating a rationing model based on clinical access rules.
- **Management simplicity:** Subscription models are often easier to set up and manage than other types of risk-sharing agreements.

Potential uses

Subscription-based models offer budget predictability for governments to fund the use of as much medicinal and diagnostic product as needed. Optimal uses for these models may include the following situations:

- **Uncertainty in utilization:** Financial uncertainty can arise where the expected number of patients is not known and therefore potential utilization is unknown. The subscription model can be used to address an emergency or a surge in demand for a product, or in cases where the utilization rate is usually consistent but there is unexpected demand (e.g., a competitor product may have an unscheduled shortage, resulting in a surge in demand for an alternative product).
- **Unmet medical need:** The subscription model is useful where there is a large unmet medical need for a new drug, but population treatment costs would be cost-prohibitive within the constraints of an annual budget due to the cost of the medication or the existence of a large patient population.
- **Add-on therapies:** A subscription approach is also useful where it is cost-prohibitive to reimburse the beneficial add-on therapy if the price of the backbone component remains the same.

A subscription model may also be useful in other situations such as those identified in the sections on portfolio agreements and amortizations agreements.

Considerations

1. Parties need to ensure that the patient population is clearly defined, because treatment populations may fluctuate dramatically over time.
2. Provincial governments may have to implement subscription agreements within their capital budgets instead of their operating budgets.
3. Pharmaceutical companies will receive payments that are not volume-based. Typically, government auditors require reimbursement programs to function as a pay-for-receipt of product or service. Public drug plans need to address the internal audit and program administration processes that require payment for receipt of product volume.
4. Given the ever-evolving treatment landscape, utilization of products may change throughout the course of the agreement lifecycle. Clauses that trigger renegotiation by either the payor or manufacturer in the event of market landscape changes, such as the introduction of a key competitor or an update in treatment guidelines, may be advisable.

Example

NHS England is testing the subscription model to incentivize pharmaceutical companies to develop new antibiotics for resistant infections. Two antibiotics that are proven to be safe and effective will be selected to undergo a National Institute for Health and Care Excellence health technology assessment throughout 2021. The government is particularly interested in antibiotics that can provide alternative treatment options for serious infections, such as bloodstream infections, sepsis and hospital-acquired pneumonia.[4]

Package agreement model

A package agreement is a holistic approach that includes auxiliary support such as data infrastructure, testing, and patient support.

Benefits

Given increasing pressures on health system budgets, a package agreement provides an opportunity for payors to reduce resource requirements and burden and enhance value from new medicines to create new programs and systems. By increasing and formalizing a framework to negotiate a package offer, payors will be able to coordinate the support they require by extracting more value via drug product negotiations. Benefits of package agreements can include the following:

- **Reduced hospital visits:** In a post-COVID-19 context, where keeping patients out of hospitals is increasingly important, patient support programs and other supports offered outside of the public system setting can enhance patient access to services and decrease hospital visits.
- **Reduced program development costs:** The benefits of a package agreement are built into a negotiation for a product, so system administrators do not have to build programs to support the introduction of a new medicine into their formularies.
- **Reduced discrepancies across provinces and territories:** Package agreements can improve equity and consistency across Canada for access to supportive services.
- **Improved long-term availability of support:** Package agreements could address payor concerns about the long-term availability of supportive services being offered once a medicine goes off patent or withdraws from the market.

[4] Elisabeth Mahase, "UK launches subscription style of model for antibiotics to encourage new development," BMJ 369 (June 2020): m2468, https://www.bmj.com/content/369/bmj.m2468

- **Improved data access:** A package agreement could include payors having some level of ownership of, or access to, the data collected. Giving payors the opportunity to own the data after the medicine has retreated from the market would address payor concerns about the longer-term continuity of such programs.

Potential uses

The range of services and other supports provided in a package agreement may be reasonably usual and customary. For example, a patient support program may manage all significant elements of the biopharmaceutical treatment in a complete multivendor outsourcing contractual arrangement. In this case, all treatments are contracted for and can include such care elements as perioperative care, assessment, evaluation and diagnostic services, pharmacotherapy, surgery, post-operative care therapeutic services, counselling, etc. The elements required in the agreement depend on both the services to be contracted and the establishment of novel business-to-business arrangements to meet the contract requirements of interest to the government and/or its service delivery agency. The following elements can be of relevance when developing a package agreement:

- **Partnerships:** A partnership of interested clinicians, diagnostic imaging companies, laboratory/nuclear medicine providers, medical device companies, information technology companies and, of course, a biopharmaceutical company can be formed to create and deliver the suite of services. In this context, government could potentially contract a not-for-profit entity to ensure both the legal and political risks are manageable.
- **Patient support programs:** Patient support programs (PSPs) typically provide a range of services including financial assistance for co-payments, compassionate drug access, nursing and other clinician services, patient navigation and even patient outcomes monitoring. A company contracts with a partner company to provide a PSP as part of a service delivery offering for a specific medication. These companies can then partner with government or private payors.
- **Capital investments:** Related to the partnership element, the not-for-profit may consider making significant investments in capital infrastructure and technologies. In such a case, the contractual provisions would need to be amenable to managing the investment risk of such an investment. This could include establishing a free-standing, non-hospital surgical facility where inpatient stays can be managed.
- **Novel contracting provisions:** The traditional item-by-item contract negotiation system may not be appropriate to achieve the clinical and financial objectives of all parties. Therefore, contracting tools such as case rate funding, clinical stage funding, normative

profit contracting, cost-recovery financings, etc., may be required. Service package agreements can include:

- Co-pay assistance
- Clinician services
- Reimbursement navigation
- Compassionate product provision
- Diagnostic testing — development, awareness, cost
- Procedures — setting up, resourcing, financing
- Ancillary supplies — needles, syringes, swabs, cleaning, etc.
- Medical information — dedicated phone line, physician consult, etc.
- Development of expertise — training, diagnosis, etc.
- Data collection — outcomes reporting, real-world evidence
- Digital platform — health trackers, apps, web portals, etc.

Considerations

1. The ability to implement a package agreement can vary based on province. An assessment must be done on feasibility and acceptability. Opportunities should be identified to experiment with different funding models across different budgets (oncology vs. non-oncology, health vs. innovation, etc.).
2. Compliance and legal issues must be considered prior to providing a package offer.
3. Value definition: All parties must clearly identify what is considered "value" upfront. This definition would then be applied as the standard.
4. All non-medicinal products and services needed to support this type of an agreement must be identified in advance of negotiations. Significant time may be required to execute certain components of these types of offers. Engagement with government (Health Canada, the Canadian Agency of Drugs and Technologies in Health, pCPA) should occur prior to negotiation.
5. Payors must recognize the value of the clinical and administrative supports as part of the agreement. They may be hesitant or have concerns about relying on private pharmaceutical infrastructure, since there is no guarantee that the infrastructure will be continued indefinitely.

Example

In Bulgaria, package agreements have been implemented to enable access to new medicines while working within finite resources. These agreements include covering the companion diagnostic of a medicine with a managed entry agreement.[5] However, details on which products and companion diagnostics this type of agreement has been applied to are not publicly available.

Portfolio agreement

Portfolio agreements have typically been used in hospital and regional health authority procurement processes, where a manufacturer has the opportunity to provide a portfolio value offering for a range of products. Typically, in these settings, this offering may include a mix of on-patent therapies and multisource products, where the total expected budget impact is acceptable to both the payor and the manufacturer.

Benefits

Manufacturers can customize a portfolio to meet their business objectives by protecting the value of their product while meeting the value objectives of the payor. Such agreements allow a manufacturer to make adjustments within a portfolio budget and can provide governments with the best possible value. Portfolio agreements also improve efficiency because they can eliminate the need for multiple, separate negotiations.

Potential uses

Existing and future products based can be included in portfolio agreements. There are a number of situations where existing and/or future products (based on the HTA outcome) may be included in portfolio agreements:

- **Company-wide:** Multiple products from one manufacturer can be included.
- **Product-by-product:** Products included can be from the same or different class.
- **Different organizations within a company:** A brand name product can be combined with a biosimilar, generic or diagnostic product in a single agreement.

[5] Alessandra Ferrario and others, "The implementation of managed entry agreements in Central and Eastern Europe: findings and implications," PharmacoEconomics 35 (2017): 1271–1285, http://dx.doi.org/10.1007/s40273-017-0559-4

Considerations

1. Assessments must be conducted with respect to feasibility and acceptability, since this type of agreement may span different provincial drug budgets. There may also be cases where the treatment is either a single product or a short course of care, and therefore the service has been provided within a government's annual operating budget, but reimbursement for the treatment is spread across more than one budget year. This would also include agreements that might involve more than one program.

2. Or service budget (e.g., the cancer agency and the health ministry drug plan). By way of example, there may be a product that can be used to treat a cancer but also used to treat a condition such as Crohn's disease. A mechanism could be developed to enable a portfolio opportunity where the benefits of the arrangement are appropriately experienced by two different drug programs, which may also have different eligible patient pools (e.g., Ontario Public Drug Program and Cancer Care Ontario).

3. Compliance and legal issues must considered prior to providing a portfolio approach.

4. In situations where there is a desire to look at a portfolio approach for newer products, challenges could include:
    a. Lack of HTA review; and/or
    b. Complexity of reviewing the value of individual components

    For example, a manufacturer may have six different launches in a year (e.g., two new products, each with three different indications). These cases could be more complex, but for areas of unmet need a portfolio approach could speed up access for patients who need these therapies. The possibility of a portfolio approach should be discussed with pCPA prior to negotiations. If products are pre-HTA recommendation, considerations should be given to determine whether a portfolio agreement would result in a different HTA recommendation outcome.

5. There are also situations where a manufacturer has a new product and is willing to consider a portfolio approach with existing products that have already been funded. In these cases, manufacturers should start assessing what a portfolio agreement could look like prior to a negotiation and have a conversation with pCPA on the openness of this approach.

6. Provincial drug programs have to account for operational spending in a line-by-line way tied to a specific drug. This can make it difficult to implement portfolio offers that span different line items. Administrators can address this challenge by linking the list of drugs in the portfolio agreement.

7. Payors are typically opposed to including products that are near their loss of exclusivity, as they wish to promote the use of generics and biosimilars. However, there is the potential for agreements where the "step-down" price for a drug that loses patent protection is negotiated in advance. In such cases, reliable information is available to determine a reasonable price reduction in advance.

Opportunities

The following are a few examples of situations that provide valuable opportunities to implement some of the various options for innovative agreements explored in this paper.

Number of products or services within a portfolio

When parties cannot agree on the value of a single product, manufacturers may consider providing more value by including other products, indications and services as part of a portfolio agreement. This allows the value offering to be spread across multiple areas to preserve value within a certain budget.

Budget management across multiple areas is an important factor in a portfolio agreement. Offering multiple products and services may be beneficial for manufacturers to protect value within the product. However, this may raise issues for payors when value is spread across different budgets (e.g., oncology vs. non-oncology).

Future considerations will be required to ensure that value is maintained for the life of the agreement in the case of loss of exclusivity of products within the portfolio agreement, so that services are maintained for the life of the product and that value is preserved if a product is divested.

Multiple drug combination therapies

An innovative agreement may be considered for combination therapies or where there are multiple products within the same therapeutic class. The products may be from a single manufacturer or different manufacturers. All component products in the combination therapy may be new, or the combination therapy may consist of a previously approved product(s) as part of a new combination therapy. This option may be considered for a prescription drug combined with one or more of the following: another prescription drug, an over-the-counter drug, a device or a diagnostic. Manufacturers should consider the benefit of a single prescription for all components in a combination therapy.

New reimbursement models are needed where the add-on or combination will extend the effects of a backbone treatment component. Current reimbursement models can make the add-on therapy cost-prohibitive if the price of the backbone component remains the same. In those cases, manufacturers may choose not to seek reimbursement or develop combination therapies that have a positive patient impact. Alternative agreements, such as a subscription model, may be considered as way to provide patient access. Manufacturers can consider a subscription model or other type of agreement that may or may not include indication-specific pricing, treatment duration caps for the backbone component of the combination, or a proportionate share of incremental value. Possible therapeutic areas where a subscription model could be used for combination therapies or for multiple products within a class include high-cost cancer therapies or add-on therapies, antivirals for HIV or HCV, or antibiotics used to treat a particular condition.

Where there are multiple manufacturers with rights in a component of a combination therapy, these arrangements should be carefully planned at the research and development stage. Manufacturers should consider whether appropriate agreements (e.g., joint venture or in-licensing,) are in place while being mindful of competition law compliance issues. It may be beneficial to consider product in-licensing arrangements where a single manufacturer can obtain market access for a combination therapy in a single prescription.

Where two or more manufacturers have rights to a component of the combination — for example, where a new combination therapy uses a previously approved product and there is no in-licensing arrangement in place — manufacturers will likely need to consider negotiating these types of value arrangements through multi-party negotiations with the pCPA.

Manufacturers should also engage with the pCPA early to discuss the desired plan for reimbursement, particularly where the combination involves a non-prescription drug (e.g., over-the-counter, device or diagnostic component) and where there is more than one manufacturer with rights to the combination.

Assurances on desired performance

Discussions regarding innovative agreements are often exclusively focused on promising drugs that receive marketing authorization with limited data or on the need to measure either hard outcomes or outcomes used in trials. However, there are opportunities to leverage innovative agreements to promote an evolution towards value-for-money pricing for drugs by reviewing a drug's performance in different ways (i.e., research-quality data collection may not be required).

Public payors face significant fiscal challenges and sometimes cannot afford to pay prices even for drugs where clinical efficacy is certain. Even prices for the rare drugs deemed "cost-effective" by HTA organizations are negotiated to improve affordability. Budget caps or higher rebates with increasing volume are frequently considered in these circumstances. Some manufacturers are, understandably, reluctant to offer the discounts sought by public payors for products that have proven their value. Furthermore, when there is a relatively accurate measurement of budget impact (i.e., little uncertainty regarding uptake), budget caps do not drive much value for payors.

In some instances, patients may not achieve the same outcomes as seen in clinical trials due to various real-world factors (e.g., adverse reactions, poorly managed dosing or poor adherence). Performance-based pricing could optimize price for manufacturers when drugs are taken as they should while payors are provided risk mitigation for situations where this is not the case.

Conclusion

As a result of significant advancements in science, including the availability of transformative curative therapies and gene therapies, new medicines and treatments are a reality for patients. These new transformative cures and innovations enable Canadians living with serious, and at times life threatening, diseases to live longer and more productive lives. Moreover, many of the new therapies deliver significant savings to other parts of the healthcare system by reducing and even eliminating expensive and traditional healthcare interventions, including lengthy and repeated hospital stays, in addition to broader positive societal impacts for patients and their families.

Both manufacturers and the pCPA recognize that innovative agreements provide an alternative approach that can support the adoption of new and innovative medicines while also achieving greater value for publicly funded programs and patients through the combined negotiation power of participating pCPA jurisdictions. Innovative agreements offer the opportunity to enhance current approaches to achieve the common objective of providing Canadian patients with access to the best medicines.

Taking into consideration the unique elements of the Canadian context, this document outlines a framework to assess several types of innovative agreements and when these approaches may be best applied. The industry recognizes public payors face significant fiscal pressures and uncertainties that have been further amplified by the COVID-19 pandemic. In this context, this framework anticipates key considerations from the perspective of payors looking at the challenges and opportunities of each type of innovative agreement and identifies which category of treatments may be most suitable for each approach.

Although there are many examples of innovative agreements in other countries, examples in Canada are limited. This may be because of a reluctance to discuss the nature of the agreements in Canada due to confidentiality concerns. To better understand the possibilities that exist in Canada, it is important that payors and manufacturers are able to share and learn from their experiences with innovative agreements. Confidential commercial terms must remain confidential but sharing general frameworks and approaches to complex problems will help expand the knowledge base, thereby improving access to new therapies to the great benefit of patients. In advancing this framework, the industry looks forward to engaging the pCPA in a dialogue to work collaboratively to better identify when it is best to use innovative agreements, the elements needed to support these innovative agreements, and which treatments would be best suited for these innovative approaches. The industry looks forward to further input and discussions with pCPA on this important topic.