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Government development of 'made-in-Canada' CAR-T cell immunotherapies: assessing cost, risk, access, and alternatives

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ABSTRACT

Summary: Chimeric Antigen Receptor T, or CAR-T cell immunotherapy, is a novel treatment that genetically engineers a patient's own T-cells to recognize and attack cancer cells. CAR-T therapeutics have been available in the United States since May 2017, and in Canada since September 2018. As of July 1, 2024, six CAR-T products had been authorized for marketing by both the U.S. Food and Drug Administration (FDA) and Health Canada. One drug was later withdrawn from the Canadian market. Health technology assessment (HTA) is a prerequisite of the public reimbursement process in Canada and is conducted by the Canadian Drug Agency (CDA), formerly known as the Canadian Agency for Drugs and Technologies in Health (CADTH). The five commercially available CAR-T products were recommended for public reimbursement by CDA. However, the prices for these therapies exceeded the cost effectiveness threshold used by CDA and therefore its recommendations were conditional on pricing adjustment. CAR-T has been eligible for public funding under US Medicare since 2017. By contrast, as of July 1, 2024, only six of the 10 Canadian provinces have authorized CAR-T products for public reimbursement. Lack of public funding is a significant barrier to accessing CAR-T immunotherapy, in addition to several other obstacles to treatment affecting patient access. Federal and provincial governments have been reluctant to extend funding eligibility for commercial products, preferring instead to invest in public development of a made-in-Canada capacity for manufacturing CAR-T therapies. Alternative funding models could more efficiently and more immediately improve access using commercially available CAR-T therapies in Canada.

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Introduction

Chimeric Antigen Receptor T, or CAR-T cell immunotherapy, is a novel cancer treatment. Lack of public funding is a significant barrier to accessing CAR-T immunotherapy, in addition to several other obstacles to treatment affecting patient access. Federal and provincial governments have been reluctant to extend funding eligibility for commercially available products, preferring instead to invest in public development of a made-in-Canada capacity for manufacturing CAR-T therapies. Using publicly available data and documents, this paper outlines the regulatory, HTA, and reimbursement status of CAR-T cell therapy in Canada. It discusses the limits of existing methods for assessing the value of CAR-T, and critically analyzes the strategy of building local manufacturing capacity instead of funding commercially available CAR-T therapies. It concludes with a discussion of alternative funding models that could more efficiently and more immediately improve access.

Characteristics of CAR-T cell immunotherapy

Chimeric Antigen Receptor T, or CAR-T cell immunotherapy, is a novel treatment that genetically engineers a patient's own T-cells to recognize and attack cancer cells. CAR-T cell immunotherapy generally works via several steps: First, T-cells are extracted from the patient's blood. Second, these T-cells are then sent to a biomanufacturing centre where they are genetically engineered to produce chimeric antigen receptors (CARs) on their surface. These receptors can recognize and bind to specific proteins, called antigens that are found on cancer cells. Third, once sufficient CAR-T cells are produced (a process which takes 3 to 4 weeks), they are transferred back into the patient. These CAR-T cells will then search and destroy those cancer cells that expresses the targeted antigen. [Ayala et al 2024]

CAR-T can be used to treat a range of blood cancers with evidence showing durable remissions and high response rates. In addition, CAR-T cells can continue to persist in the body long after treatment and therefore have the potential to fight cancer for the longer term. There are many active clinical trials of CAR-T cell therapy candidates targeting both hematological malignancies and solid tumors [Wang et al 2023] and autoimmune diseases like lupus erythematosus [Mackensen et al 2022]. CAR T-cell therapy can be associated with serious side effects including cytokine-release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS), tumor lysis syndrome (TLS), anaphylaxis (life-threatening allergic reaction), B-cell aplasia, and infection. [Sterner and Sterner 2021]

Commercially available CAR-T products

The first CAR-T therapeutic (KYMRIAH) was approved in the United States in May 2017, and in Canada in September 2018. As of July 1, 2024, six CAR-T products had been authorized for marketing by both the U.S. Food and Drug Administration (FDA) and Health Canada. However, one product (ABECMA) was cancelled premarket in Canada in November 2023. The lag time between US FDA and Health Canada approvals for the five remaining commercially available products ranged from 319 days to 483 days (more than 366 days on average). [TABLE 1]

TABLE 1. CAR-T therapies authorized for marketing in the United States and Canada, July 1, 2024.

CAR-T therapy	Ingredients	Manufacturer	Country	First Approval	Lag Time [Days]
ABECMA	idecabtagene vicleucel	Bristol Myers Squibb	USA	26-Mar-21	
		Celgene	CAN	*26-May-21	*
BREYANZI	lisocabtagene maraleucel	Bristol Myers Squibb	USA	02-May-21	
		Bristol Myers Squibb	CAN	06-May-22	369
CARVYKTI	ciltacabtagene autoleucel	Johnson & Johnson	USA	28-Feb-22	
		Johnson & Johnson	CAN	09-Feb-23	346
KYMRIAH	tisagenlecleucel	Novartis	USA	30-May-17	
		Novartis	CAN	05-Sep-18	463
TECARTUS	brexucabtagene autoleucel	Kite	USA	24-Jul-20	
		Gilead	CAN	08-Jun-21	319
YESCARTA	axicabtagene ciloleucel	Kite	USA	18-Oct-17	
		Gilead	CAN	13-Feb-19	483

Sources: Health Canada (2024). Notice of Compliance (NOC) Database, and Drug Product Database. | U.S. FDA Office of Therapeutic Products (OTP). | Notes: * cancelled pre-market 14 Nov 2023.

CAR-T cell immunotherapy cancer indications

As of July 1, 2024, there were 11 known unique indications that can be treated with CAR-T cell immunotherapy products including: Multiple myeloma (MM), chronic lymphocytic leukemia (CLL), small lymphocytic lymphoma (SLL), large B-cell lymphoma (LBCL), diffuse large B-cell lymphoma (DLBCL), high-grade B-cell lymphoma (HGBL), follicular lymphoma (FL), mantle cell lymphoma (MCL), primary mediastinal large B-cell lymphoma (PMBCL), and acute lymphoblastic leukemia (ALL). The U.S. FDA approved indications, and Health Canada approved indications are listed in TABLE 2.

TABLE 2. Approved indications for CAR-T cell immunotherapy, US FDA and Health Canada, July 1, 2024.

CAR-T therapy	US FDA	Health Canada
ABECMA	MM (adults)	*MM (adults)
BREYANZI	CLL or SLL	
	DLBCL or HGBL	
	FL (adults)	
	LBCL (adults)	LBCL (adults)
	MCL (adults)	
CARVYKTI	MM (adults)	MM (adults)
KYMRIAH	ALL (children and young adults)	ALL (children and young adults)
	DLBCL or HGBL	DLBCL or HGBL
	FL (adults)	FL (adults)
	LBCL (adults)	LBCL (adults)
TECARTUS	ALL (adults)	ALL (adults)
	MCL (adults)	MCL (adults)
YESCARTA	DLBCL or HGBL	DLBCL or HGBL
	FL (adults)	FL (adults)
	LBCL (adults)	

Sources: Health Canada (2024). Notice of Compliance (NOC) Database, and Drug Product Database. | U.S. FDA Office of Therapeutic Products (OTP). | Notes: * cancelled pre-market 14 Nov 2023. Multiple myeloma (MM), chronic lymphocytic leukemia (CLL), small lymphocytic lymphoma (SLL), large B-cell lymphoma (LBCL), diffuse large B-cell lymphoma (DLBCL), high-grade B-cell lymphoma (HGBL), follicular lymphoma (FL), mantle cell lymphoma (MCL), primary mediastinal large B-cell lymphoma (PMBCL), acute lymphoblastic leukemia (ALL).

Health Technology Assessment (HTA)

Commercially available CAR-T therapies in Canada are subject to health technology assessment (HTA) as a prerequisite of the public reimbursement process. HTA is conducted by the Canadian Drug Agency (CDA), formerly known as the Canadian Agency for Drugs and Technologies in Health (CADTH) on behalf of all federal, provincial, and territorial publicly funded drug plans, except Quebec which has its own provincial HTA agency.

As of July 1, 2024, five of the six commercially manufactured CAR-T products had been recommended for public reimbursement by CDA. One product (ABECMA) was not recommended for public reimbursement (and was later withdrawn from the market), and two products were currently undergoing active HTA evaluations. [TABLE 3]

Data show that the time spent by the CDA to review and issue recommendations on the submissions for the eight indications across the five commercially available CAR-T therapies ranged from 194 days to 324 days, averaging 234 days. [TABLE 3]

All submissions for the seven indications across the five commercially available CAR-T products received positive recommendations for public reimbursement with clinical criteria and/or conditions. Prices for these therapies exceeded the cost effectiveness threshold used by CDA and therefore its recommendations were conditional on severe pricing adjustment. [TABLE 3]

TABLE 3. Canadian Drug Agency HTA recommendations for commercially available CAR-T therapeutic products, July 1, 2024.

CAR-T therapy	Indication	Recommendation	Submission	Completion	Wait (days)
ABECMA	MM	DNR	16-Dec-20	12-Nov-21	331
BREYANZI	DLBCL, HGBL	RCCC	9-Aug-21	29-Jun-22	324
BREYANZI	DLBCL, HGBL	-	8-May-24	active	-
CARVYKTI	MM	RCCC	23-Sep-22	1-May-23	220
CARVYKTI	MM	-	18-Apr-24	active	-
KYMRIAH	FL	RCCC	1-Feb-23	1-Sep-23	212
KYMRIAH	*DLBCL, *HGBL	n/a	-	-	-
KYMRIAH	*ALL	n/a	-	-	-
TECARTUS	ALL	RCCC	16-Sep-22	29-Mar-23	194
TECARTUS	MCL	RCCC	18-Dec-20	24-Aug-21	249
YESCARTA	FL	RCCC	13-Apr-23	2-Nov-23	203
YESCARTA	DLBCL, HGBL	RCCC	9-Jun-22	3-Feb-23	239

Sources: Canadian Drug Agency (2024). * Confirmed by manufacturer. Notes: n/a = Data not available from CDA, DNR = Do not reimburse, RCCC = Reimburse with clinical criteria and/or conditions. Multiple myeloma (MM), chronic lymphocytic leukemia (CLL), small lymphocytic lymphoma (SLL), large B-cell lymphoma (LBCL), diffuse large B-cell lymphoma (DLBCL), high-grade B-cell lymphoma (HGBL), follicular lymphoma (FL), mantle cell lymphoma (MCL), acute lymphoblastic leukemia (ALL), primary mediastinal large B-cell lymphoma (PMBCL).

For example, in its reimbursement recommendation for KYMRIAH, the CDA stated that the product should be reimbursed by public drug plans for the treatment of adults with relapsed or refractory follicular lymphoma (FL) if the cost is reduced. The agency suggested that price reductions of 71-82% would be required for the CAR-T therapy to be considered cost-effective. [Canadian Drug Agency 2023]

FL is a common type of lymphoma that develops when the body makes abnormal blood cells that cluster together to form lumps in lymph nodes or other tissues. CDA acknowledged evidence showing that treatment with KYMRIAH resulted in durable responses and that it may improve overall survival time and the time until disease progression or death, and that it may be an effective treatment option for patients. [Canadian Drug Agency 2023] However, the CDA concluded that "Kymriah does not represent good value to the health care system at the public list price. A price reduction is therefore required." [Canadian Drug Agency 2023]

CDA assessments have caused protracted price negotiations between manufacturers and public payers, which has raised questions about whether HTA methods are appropriate for CAR-T therapies.

The CDA's HTA methods do not take account of the small proportional impact of drug expenditures on total healthcare spending. Based on public list prices, KYMRIAH is estimated to cost the public drug plans approximately $192 million over 3 years or about $64 million per year. [Canadian Drug Agency 2023] This means that the total cost of this CAR-T therapy is only 0.02% of the estimated $344 billion spent in total on healthcare in Canada in 2023 [Canadian Institute for Health Information 2023].

HTA methods also do not take account of the full value of CAR-T including factors like reduced need for subsequent treatments, improved quality of life, as well as the potential longer survival compared to current standard of care. CAR-T therapies can offset some downstream costs associated with complications, hospitalizations, and additional lines of treatment. A study conducted in the US found that while the total cost of the procedure was higher for CAR-T compared to stem cell transplants, the non-pharmacy costs like length of stay and ICU admissions were lower for CAR-T. The study suggests that the high upfront cost of CAR-T could be partially offset by savings from reduced complications and shorter hospital stays. [Cui et al 2022, Fiorenza et al 2020, Gye et al 2022]

Another limitation is that standard clinical trial designs are not suitable for technologies like CAR-T therapy. For example, overall survival is traditionally used as an end point in studies to determine clinical benefit, but its measurement requires long follow-up periods that can delay patient access to breakthrough therapies. To address this, the FDA allows surrogate end points in trials of hematologic cancers, such as overall response rate and progression-free survival. These end points enable small sample sizes and short study and follow-up durations. CDA does not recognize surrogate endpoints in its HTA process.

The cost-effectiveness threshold range used by CDA is not supported empirically. [Rebeira 2022] Thresholds vary significantly between jurisdictions. According to the CDA, at the time of its assessment, treatment of FL with Kymriah was expected to cost approximately $450,000 CAD, and the incremental cost-effectiveness ratio ranged from $193,516 to $434,036 CAD per quality-adjusted life-year (QALY) gained. CDA's recommendation was based on an incremental cost-effectiveness ratio of $50,000 CAD/QALY. [Canadian Drug Agency 2023] In the US, the threshold is closer to $300-400K USD/QALY. If the CDA had used the US cost-effectiveness threshold, KYMRIAH would have been recommended without price adjustment.

Public reimbursement

Following HTA, manufacturers of new drugs enter price negotiations with the pan-Canadian Pharmaceutical Alliance (pCPA), which collectively represents all federal, provincial, and territorial public drug plans. Successful negotiations result in the issuance of a letter of intent (LOI) to list the product on public drug formularies. Each jurisdiction independently decides on the timing and final terms and conditions of eligibility for public reimbursement.

According to the data published by the PCPA, as of July 1, 2024, only two (BREYANZI, TECARTUS) of the five commercially available CAR-T Products had successfully completed negotiations with the PCPA resulting in the issuance of an LOI. Two (CARVYKTI, YESCARTA) products were in active negotiation, one (KYMRIAH) was under consideration for negotiation. ABECMA was not pursuing negotiation because it had been withdrawn from the market. [TABLE 4]

Measured from the point of engagement to the issuance of an LOI, the time spent in the price negotiation process with the PCPA was 326 days for BREYANZI, 353 days for the first submission of TECARTUS, and 161 days for the second submission, averaging 280 days.

CAR-T is administered in hospital, which makes it automatically eligible for public funding in the Canadian provinces that have authorized it as a "standard of care". As of July 1, 2024, only six of the 10 Canadian provinces had authorized CAR-T therapy as a standard of care: Quebec (October 2019), Ontario (December 2019), Alberta (August 2020), Manitoba (January 2023), Saskatchewan (February 2023), and British Columbia (March 2024). By contrast, CAR-T has been eligible for public funding under US Medicare since 2017. [Hunter 2023; Government of Manitoba 2023; CBC news 2020; BC Ministry of Health 2024; US Centers for Medicaid and Medicare 2024]

Commercial CAR-T products must be specifically approved for public reimbursement by the provincial ministries of health. It is important to point out that in Quebec, Ontario, and Alberta public funding covered the cost of KYMRIAH as soon as the therapy was designated a standard of care. Reimbursement was extended without going through the CDA's HTA process, and without requiring price negotiation with the PCPA. The therapy was later submitted by the manufacturers to the CDA and the PCPA. In these three provinces, public funding for BREYANZI and TECARTUS followed the issuance of LOIs by the PCPA.

British Columbia took a different approach. The provincial government waited to develop the local capacity to manufacture CAR-T cells in BC Cancer's Deeley Research Centre before finally authorizing the immunotherapy as a standard of care in March 2024. In the meantime, authorized BC patients accessed CAR-T therapy through designated facilities and hospitals in Ontario and Alberta, with the cost of treatment being billed back to the provincial government of British Columbia. Patients from other provinces followed the same process with billings going back to their provinces.

TABLE 4. Commercially available CAR-T products negotiation status for public reimbursement with the pCPA, July 1, 2024.

Product	Manufacturer	Status	Indication	Engagement	Completion	Wait (days)
ABECMA	Celgene	Negotiations not pursued	MM	n/a	18/04/2024	
BREYANZI	Celgene	Concluded with an LOI	DLBCL, PMBCL, HGBL, FL	20/01/2023	12/12/2023	326
CARVYKTI	Johnson & Johnson	Active Negotiation	MM	10/11/2023	n/a	
KYMRIAH	Novartis	Under consideration	FL	n/a	n/a	
KYMRIAH	Novartis	n/a	*DLBCL, *HGBL	n/a	n/a	
KYMRIAH	Novartis	n/a	*ALL	n/a	n/a	
TECARTUS	Gilead	Concluded LOI	ALL	19/05/2023	27/10/2023	161
TECARTUS	Gilead	Concluded LOI	MCL	22/11/2021	10/11/2022	353
YESCARTA	Gilead	Active Negotiation	FL	14/02/2024	na	
YESCARTA	Gilead	Active Negotiation	DLBCL, HGBL	26/09/2023	na	

Source: Pan-Canadian Pharmaceutical Alliance (2024). * Confirmed by manufacturer. Notes: n/a = Data not available from pCPA. Multiple myeloma (MM), chronic lymphocytic leukemia (CLL), small lymphocytic lymphoma (SLL), large B-cell lymphoma (LBCL), diffuse large B-cell lymphoma (DLBCL), high-grade B-cell lymphoma (HGBL), follicular lymphoma (FL), mantle cell lymphoma (MCL), acute lymphoblastic leukemia (ALL), primary mediastinal large B-cell lymphoma (PMBCL).

Manufacturing CAR-T therapies

The federal and provincial governments have adopted a strategic policy of subsidizing the development of a made-in-Canada capacity for manufacturing CAR-T therapies in direct competition with private sector pharmaceutical companies under the assumption that it will improve access to CAR-T for Canadian patients, at a lower cost. The policy also reflects the strategic rationale that Canada needs to reduce its reliance on foreign multinational pharmaceutical manufacturers.

Over the last 10 years, the federal government has publicly funded BioCanRx., which was incorporated in 2014 as a not-for-profit organization, and is essentially a government-sponsored enterprise (GSE) established to provide "operational support" for "decentralized", "point of care" biomanufacturing capacity in Canada for novel therapies like CAR-T. From 2015 to 2023, BioCanRx received almost $120 million primarily from federal government sources like the National Centres of Excellence, and the Strategic Science Fund, a program of Innovation, Science and Economic Development Canada.

Several made-in-Canada CAR-T therapies are in various stages of clinical trials. However, none have been approved by Health Canada to compete with the 5 commercially available products previously mentioned.

Some research on CAR-T cell manufacturing suggests that decentralized production might be a less costly alternative to commercially available products. A German study examined the cost components of a hospital-based CAR-T cell production facility. Researchers observed that one manufacturing system had a maximum capacity of 18 products per year. If a single product was produced, fixed cost per unit was $584k USD, falling to $32k USD if 18 products were produced. They concluded that decentralized manufacturing using a nonprofit model would be feasible and less expensive than purchasing commercially available CAR-T therapies. [Ran 2020]

However, the study has several limitations, some of which are acknowledged by the authors:

- The cost calculation excluded input factors like regulatory affairs and intellectual property management, and the capital value of land, facilities and equipment of the institutional host.
- Results are not necessarily generalizable because fixed and variable costs could differ substantially between international and subnational jurisdictions.

- The analysis assumed that variable cost would remain constant.
- The study simply illustrates that production costs go down with increasing volume because of economies of scale, and scale is one of the strengths of commercial suppliers.
- The total cost of decentralized production for the first unit was $631K USD, which is higher than list prices for commercially available CAR-T therapies, and significantly above the final prices paid by public payers after negotiating rebates with manufacturers. Decentralized manufacturing centres which do not achieve sufficient economies of scale could be more costly than anticipated.
- The affordability rationale for decentralized manufacturing in a nonprofit setting is undermined by the fact that, while CAR-T therapies currently rank among the most expensive pharmaceutical products, the overall budget impact is manageable in most jurisdictions because of the small patient population.
- CAR-T therapy is a complex process requiring a high level of expertise from highly trained staff. Decentralizing production requires duplication of the expert labour costs, which could be avoided by large scale centralized manufacturing facilities.

General limitations of public, nonprofit production of pharmaceuticals

The evidence supporting the publicly owned/subsidized, nonprofit, point-of-care production model is not definitive. In general, theory and empirical studies suggest that it is a sub-optimal approach to bio-pharmaceutical manufacturing. Research on the economic performance of publicly owned/subsidized enterprises indicates that they are less efficient than competitive private sector enterprises, and more prone to business failure without continuous public subsidy. Non-profit manufacturers focus on maximizing social welfare, which tends to produce inefficient pricing. Commercial manufacturers aim for profit maximization or cost minimization, which tends to produce efficient pricing. Publicly subsidies tend to misallocate scarce capital resources, which would otherwise be invested in more productive uses. [DeWenter and Malatesta. 2001; Megginson and Netter 2001; Boubakri et al 2005]

Given the combination of factors putting downward pressure on prices, the cost of commercially available drug products most likely reflects an efficient price in Canada, which will earn sufficient profits to recover the risk adjusted capital cost of R&D and incentivize investors to fund future drug development. Some factors include:

- The list prices of new drug therapies are already subject to regulation by the Patented Medicine Prices Review Board.
- Monopsony price negotiation with the pan-Canadian Pharmaceutical Alliance, extracts manufacturer rebates averaging 36% off list prices. [Ontario Auditor General 2017]
- Manufacturers also face price pressures from competing suppliers and treatment substitutes. [Lichtenberg and Philipson 2002]
- Even when there is a single supplier, if the market is contestable, the threat of a new product entry incentivizes competitive pricing. [Baumol 1983]
- International price differentiation generally results in globally efficient prices that reflect local market conditions like price-income elasticities. [Danzon and Furukawa 2003]

The cost and risks associated with pharmaceutical R&D are significant. Generally, drug discovery and development occur over 10–15 years. The R&D cost for a new drug has been estimated to range from $314 million to $4.2 billion. [Adams 2006, 2010; DiMasi 2003, 2004, 2007, 2016; Javasundura 2019; Mestre-Fernandiz 2012; Paul 2010; Prasad 2017; Sertkava 2024; Wouters 2020] Nine out of ten drug candidates that have entered clinical studies fail to advance to marketing authorization. [Sun 2022] A general strategy of producing pharmaceuticals through publicly funded non-profit entities will shift the R&D costs and risk onto taxpayers. Canadians would not likely tolerate the use of public money to underwrite the failure rate associated with pharmaceutical R&D, and it is unlikely that governments could survive the political consequences if serious adverse reactions happen to occur to patients taking prescription drugs developed with public funds.

Sourcing the supply of pharmaceuticals to the Canadian market through foreign multinational companies, creates an opportunity to benefit from comparative advantage, which is an economy's ability to produce a particular good or service at a lower opportunity cost than its trading partners. [Riccardo 1821] Instead of trying to build new bio-pharmaceutical manufacturing capacity with public funding, it would be more efficient for Canada to remove disincentives to investment generally, allowing capital to flow to where it has a comparatively lower opportunity cost, and public payers should simply purchase the products made more productively by our trading partners.

Policy alternatives

Denying or delaying public funding for commercially available CAR-T products is not a viable policy. Blocking patient access to these therapies is an unethical approach to price negotiation and cost control, because it can have grave health consequences including premature mortality. For the reasons previously discussed, developing and manufacturing CAR-T therapeutics through a publicly subsidized, government sponsored/ or owned, nonprofit organization in competition with private sector manufacturers is less optimal than simply making commercially available products eligible for public reimbursement. There are several alternative policy approaches for managing the high cost of CAR-T cell therapy, some of which are briefly described below.

Outcome-Based Agreements

Payments for CAR-T are tied to the actual clinical outcomes achieved by the therapy for that patient. For example, if the therapy delivers the expected level of benefit, either remission or survival improvement, then payment is made in full. However, if the benefits cannot be achieved, the payment will either be reduced or adjusted as negotiated in advance. In addition, options can be considered where discounts are offered based on efficacy or the number of patients treated. If the therapy demonstrates superior outcomes compared to its competitors or standard of care, the magnitude of discounts can be adjusted.

Performance-Based Contracts

In this model, the agreement includes an arrangement where the cost of the therapy is contingent on achieving very specific performance metrics, such as a specific duration of remission.

Coverage with Evidence Development (CED)

This represent another form of agreement where coverage is contingent upon the collection of additional evidence and data to confirm the effectiveness of the CAR-T cell immunotherapy over time for each of the patient. The coverage can then be adjusted based on this new evidence.

Conditional Reimbursement

Under conditional reimbursement models only some initial costs are covered, but additional payments are contingent upon achieving predefined clinical outcomes or other milestones. This represents another way to ensure alignment of costs with actual value provided to the patients by CAR-T.

Risk-Pool Funds

A fund is set up where costs are pooled among various stakeholders (e.g., government, manufacturers, private insurers, hospitals) to cover all the costs of treatment using CAR-T cell immunotherapy. The approach attempts to distribute the financial risk of the therapy very similar to how insurance companies operate.

Shared Savings Models

For this type of model, both the payers and manufacturers share the financial risk as well as savings associated with the therapy. The financial risk is borne by both parties and If CAR-T cell immunotherapy results in downstream cost savings compared to standard of care treatments over the life of the patient, then both parties can also share in these savings.

Amortized Payment Installments

This approach allows payment for CAR-T cell immunotherapy in installments rather than one lump sum enabling the high upfront costs to be made more affordable by distributing the costs over a longer period of time.

Deferred Payment Plans

Payments here are deferred until certain pre-specified outcomes are achieved with different possible financing opportunities incorporated.

Flat Fee Agreements

This is a subscription-based model where a fixed fee is paid for a certain period or number of treatments, regardless of the patient's treatment costs. The approach helps to provide more predictable costs and especially help to facilitate budget planning for healthcare systems.

Conclusion

Canada experienced significant delays to access CAR-T therapies, due to regulatory approval (Canadians waited 366 days longer than Americans), health technology assessment (in process 234 days on average), and public reimbursement negotiations (in process 257 days on average). Despite strong clinical evidence for the efficacy of CAR-T therapies, and the manageable overall impact on health budgets, provincial governments have been reluctant to pay for commercially available treatments due to high prices. The two most significant policy solutions to these challenges, concern the need for more flexible HTA methods for high-cost therapies like CAR-T; and consideration of alternative reimbursement models that could expand access to CAR-T therapy and reduce the time to access treatments which are already commercially available.

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