LYMPHOMA CANADA | LYMPHOME CANADA

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SUBJECT: Improving access to innovative cancer therapies in Canada – Lymphoma patients

Dear intended recipients,

Health Canada, Canada's Drug and Health Technology Agency (CADTH), Institut national d'excellence en santé et en services sociaux (INESSS), the pan-Canadian Pharmaceutical Alliance (pCPA), and provincial funding bodies have separate processes to ensure the safety and efficacy of oncology drugs, and feasibility of implementation. However, these sequential review processes are time-consuming and burdensome, resulting in long delays for much-needed therapies. Innovative oncology drugs hold remarkable potential to transform treatment and increase survival, especially in advanced stage patient populations. Though current work is underway to increase innovative therapies through optimizing and streamlining drug review protocols, there is little effort focused on timely and effective implementation strategies of oncological therapies. The review of smaller non-randomized or non-comparative trials in specific circumstances, is one way timely and effective review can greatly impact unmet patient needs.

Canadian lymphoma patients need your help in ensuring that they are provided with equitable and timely access to life-saving cancer therapies. Currently, there are disparities in available treatments depending on which province or territory a lymphoma patient resides in. Every Canadian deserves the opportunity to receive the best quality healthcare, including local access to **all** Health Canada approved lymphoma therapies with minimal delay.

What is Lymphoma and why is early treatment important?

Lymphoma is a cancer of the lymphatic system, where cancerous lymphocytes travel and grow throughout the lymphatic system, including the lymph nodes, spleen, and bone marrow. There are more than 80 different subtypes of lymphoma falling under the umbrella of two major categories, Hodgkin lymphoma (HL) and Non-Hodgkin lymphoma (NHL). Both major categories are further subdivided into several subtypes, which each have their own specific set of treatment options, follow-up care and management. Early diagnosis and treatment are crucial to ensure the best prognosis and quality of life for patients. Significant delays in diagnosis or treatment can be fatal for those living with lymphoma.

Importance of Access

Timely access to all approved therapies is crucial in improving patient response to treatment, maximizing quality of life, and decreasing chances of relapse. Lymphoma patients need access to a variety of treatment options to make important decisions with their healthcare team regarding length of treatment, side effects, and route of administration. A lymphoma diagnosis takes an immense toll on the physical and mental health of patients and their loved ones, and further burden should not be placed on individuals due to inequities and challenges in accessing medical treatment within a patient's home province.

Inequities

Based on thorough research of the existing Lymphoma and CLL therapies in Canada, inequities in access to and funding therapies was observed across the different provinces and territories. These challenges include but are not limited to delayed access to therapy compared to individuals in other provinces, financial challenges to afford therapy that is not covered publicly, and/or challenges associated with having to travel for treatment including lack of support, financial implications, and lack of adequate follow-up care after their return.

CADTH & INESS Recommendations

A positive/conditional recommendation from CADTH or INESS is a critical component in ensuring public access to lymphoma therapies in Canada. Criteria listed by CADTH for positive recommendations include significant unmet patient need, lack of existing safe and effective treatment options, small patient population, and infeasibility for randomized control trial (RCT) in the target population [1]. Criteria resulting in a negative CADTH recommendation include: uncertainty of net clinical benefit due to non-comparative data, ongoing RCT, and feasibility to conduct RCT in target population [1]. If a negative recommendation is issued by CADTH "this slows down, if not essentially halts the path to public access for new therapies, since pCPA will generally not consider negotiations for such a drug"[1]. This creates delays in access as the therapy will no longer enter the price negotiation phase [1]. Should re-submission occur at a later point as more clinical evidence becomes available, "this may still result in delays of up to 515 days to access innovative therapies if approved the second time around" [1]. This delay severely

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impacts patients at advanced stages of the disease, "resulting in patients either not receiving treatment or requiring very sick patients to travel outside of Canada to receive therapy, paying out of pocket, and further increasing their burden" [1]. Hence, "transparency in the CADTH evaluation framework for limited datasets is essential for stakeholders to tailor their applications to meet the appropriate criteria for innovative therapies to become readily and equitably accessible to Canadian patients" [1].

The French equivalent of CADTH, INESSS, is responsible for reviewing and providing a recommendation for lymphoma therapies for Quebec residents. Both CADTH and INESSS collaborate on select health technology assessments but have independent review boards and processes which examine clinical, economic, and patient information for each oncology drug. Unfortunately, there can be differences in recommendations between CADTH or INESSS where one organization gives a positive recommendation, and the other does not. This recently occurred for tafasitamab (Minjuvi), a monoclonal antibody therapy used in combination with lenalidomide, an immunomodulatory drug, for the treatment of relapsed/refractory (R/R) diffuse large B-cell lymphoma. In October of 2022, CADTH did not recommend this therapy be reimbursed by public drug plans, whereas INESSS issued a positive recommendation for the province of Quebec in November 2022. This contributes to variable funding between Canadian provinces for novel therapies and further challenges for lymphoma patients that require therapy not accessible to them.

Price Negotiations

In terms of timely access, significant delays in the approval process or price negotiations are costly to lymphoma patients. As highlighted in our White Paper Report, the entire process from research and development to marketing of effective and innovative therapies can take over ten years. Once the pCPA, an alliance of provincial, territorial, and federal governments, determines that the therapy will enter the price negotiation phase, the non-transparent nature of negotiations often leads to delays in quick and equitable access to new drugs in Canada [1]. This is largely because negotiations are not bound by any mandatory time frames in terms of completion, and "the specific criteria involved in decision-making, review timelines and the negotiation process are not shared publicly" [1]. This as an issue as delays in negotiations have dire consequences, including patients being ineligible to receive lifesaving therapies.

Interprovincial Inequalities – Access to treatment

After the negotiation process, each province and territory develop their own product listing agreement with the manufacturer, and they can refuse to list the drug in their formulary or establish different terms of access [1]. This creates interprovincial inequities in treatment as some provinces will have higher compliance with the recommendations [1]. Recent examples of lymphoma therapies that have been approved by CADTH but have variable funding across Canadian provinces include pembrolizumab and nivolumab for the treatment of relapsed/refractory Hodgkin lymphoma and polatuzumab vedotin for the treatment of relapsed/refractory diffuse large B-cell lymphoma. There are also significant delays with provincial funding decisions amongst higher-priced therapies with significant clinical benefits, as is the case for CAR-T Therapy in Canada. In November 2022, the pCPA reached an agreement to reimburse brexucabtagene autoleucel (Tecartus), a CAR T-cell therapy for Mantle Cell Lymphoma, after a positive CADTH recommendation in August of 2021 and Health Canada approval in June of 2021. This example highlights a significant delay in provincial funding negotiations, with the final letter of intent posted a year after the pCPA issued a letter of engagement to reimburse this CAR T-cell therapy.

Chimeric Antigen Receptor T-Cell Therapy, or CAR-T therapy, is a promising and innovative treatment option for some lymphoma patients in Canada. It is a type of immunotherapy that improves the effectiveness of T-cells, a type of cell in your body that plays a central role in the immune response. These T-cells are extracted, re-engineered, and then administered back into the same patient, helping to specifically target and kill cancerous lymphoma cells.

CAR-T therapy was initially approved by Health Canada in 2018 for relapsed and refractory Diffuse Large B-Cell Lymphoma (DLBCL) patients. Inequitable access to this therapy remains to be a major barrier in Canada, as it is only currently locally accessible for patients that live in Ontario, Quebec, Alberta, Saskatchewan, and Nova Scotia. This means that patients in other provinces cannot receive this treatment and must instead travel out of province or the United States to access it. It is devastating for those that feel unwell to travel, that do not have a designated caregiver required for out of province travel to receive CAR-T therapy or that need additional financial support to travel, as many patients in this scenario have no other treatment option and are considered palliative.

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Having local access is **vital** for patients as:

- The patient can remain close to their family/friend support group and network
- The patient will have proper follow-up care with their treating physician
- There are limited financial impacts and more supports available locally
- There is a reduced risk of Covid-19 exposure and other infections due to travel

In the case of travelling for CAR-T therapy, patients must stay away from their home for several weeks – for blood sampling, during infusion and through the observation period. This is extremely disruptive for patients and caregivers, as many cannot afford the travel and commitment necessary for treatment. For provinces that do have the capacity to facilitate CAR-T cell treatment, there is a limit to the number of lymphoma patients that can be referred to their center. Approximately 60 patients per province can access CAR-T on a yearly basis [4]. This greatly restricts the number of people who get access to life-saving treatment.

Charlotte is one of the lucky patients who was able to receive CAR-T therapy close to home at Princess Margaret Cancer Centre, to treat her relapsed Diffuse Large B-Cell Lymphoma. She wouldn't likely be here today if she could not access to CAR-T through a clinical trial. Charlotte recognizes the challenges that lymphoma patients throughout Canada can face, as she "couldn't imagine how challenging life and cancer treatment would have been if she lived far away from the hospital and didn't have the support of her family". As a result of this therapy, Charlotte "wakes up every morning happy to experience another day of life" and looks forward to her upcoming trip to Florida to celebrate her 70th birthday, 7 years after her initial diagnosis.

Final remarks

In summary, progress has been made, but much work remains to be done to ensure that Canadian lymphoma patients and all cancer patients can gain access to new and effective therapies in a timelier manner. Otherwise, patients may continue to face the following when it comes to accessing therapies in Canada:

1. Lack of local access to new cancer drugs that are approved in other provinces/territories
2. Lack of access to novel drugs funded due to differing provincial eligibility requirements
3. Lack of full public coverage for therapies, with financial concerns of travel or treatment related costs

At Lymphoma Canada, we appreciate the complexity of the decision-making process and changes that have been made to create new infrastructure to improve processes in the approval and delivery of new therapies. However, we continue to call on the Canadian government and regulatory agency, health and technology assessment agency and provincial funding agencies to collaborate to continue our vision to provide solutions to improve the untimely access to cancer therapies in Canada. Our patients are counting on you. We encourage you to visit our White Paper Report that provides further detail on inequities in accessing lymphoma treatment in Canada.

Regards,

Antonella Rizza, CPA, CA

CEO

Lymphoma Canada

References:

[1] Lymphoma Canada. (2021). *2021 Update to the 2018 White Paper: Improving Access to Innovative Cancer Therapies in Canada*. Retrieved January 27, 2023, from https://www.lymphoma.ca/wp-content/uploads/2021/12/20210804-LC-White-Paper_WEB_v2.pdf