

CADTH Reimbursement Review

Patient Input

brexucabtagene autoleucel (TBC)
(Gilead Sciences Canada Inc.)

Indication: For the treatment of adult patients with relapsed or refractory (r/r) mantle cell lymphoma (MCL) who have received treatment with a Bruton's tyrosine kinase inhibitor (BTKi).

CADTH received patient input from:
Lymphoma Canada

January 22, 2021

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CADTH Reimbursement Review Patient Input Template

Name of the Drug and Indication	Brexucabtagene Autoleuclel for adult patient's with relapsed/refractory mantle cell lymphoma who have received treatment with a Bruton's tyrosine kinase inhibitor
Name of the Patient Group	Lymphoma Canada
Author of the Submission	████████████████████
Name of the Primary Contact for This Submission	████████████████████
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1. About Your Patient Group

Lymphoma Canada is a national Canadian registered charity that empowers the lymphoma community through education, support, advocacy, and research. Based out of Toronto (ON), we collaborate with patients, caregivers, healthcare professionals, and other organizations and stakeholders, to promote early detecting, find new and better treatments for lymphoma patients, help patients access those treatments, learn about the causes of lymphoma, and working together to find a care. Resources are provided for both English and French Canadians. For more information about our organization, please visit us at www.lymphoma.ca

2. Information Gathering

Lymphoma Canada (LC) conducted an anonymous online survey of Mantle Cell Lymphoma (MCL) patients between October 19 2020 – January 11, 2021. Links to the surveys were sent via e-mail to patients registered through the LC database. The links were also made available via LC Twitter and Facebook accounts, Canadian and American Cancer Society message boards, Facebook groups organized for lymphoma patients and survivors, physician specialists across Canada, physicians at leading clinical trial sites across the United States of America (USA), and international lymphoma organizations' individual contacts. The survey involved a combination of multiple choice, rating and open-ended questions. Skipping logic was built into surveys so that respondents were asked questions only relevant to them. Open-ended responses to surveys that reflected the sentiment of a majority are included verbatim to provide a deeper understanding of patient perspectives.

There were 33 patients that provided input on their experience with their MCL, with only 1 of these patient's able to provide their experience with the Brexucabtagene Autoleuclel (BXA) therapy. As there were no clinical trial sites in Canada where patient's could gain access to this treatment, sampling was

required from the USA population to retrieve information on the patient experience. LC had a tremendous difficulty finding patients despite significant effort by LC staff. There were no caregivers that participated in this survey. Of patients who provided their demographic information (see **Tables 1 and 2**), the majority lived in Canada, >50% are male, and are over the 44 years of age.

Table 1: Country of survey respondents (33 respondents)				
Respondents	CAN	USA	Skipped	Total
Patients <u>WITHOUT</u> BXA experience	24	0	8	32
Patients <u>WITH</u> BXA experience	0	1	0	1

Table 2: Gender and age of survey respondents									
Respondents	Age Range						Gender		
	<44	45-54	55-64	65-74	75-84	skipped	Female	Male	Skipped
Patients <u>WITHOUT</u> BXA experience	0	5	6	10	2	9	9	14	9
Patients <u>WITH</u> BXA experience	0	0	0	1	0	0	0	1	0

3. Disease Experience

Patients were asked to rate which symptoms had the greatest impact on their quality of life at diagnosis, on a scale from 1 to 10, 1 being No Impact to 10 being Significant Impact. 33 patient respondents rated the top three symptoms causing the greatest impact were enlarged lymph nodes (4.8), fatigue (3.7), and indigestion/abdominal pain/bloating (2.9), high white blood cell counts (2.2), and low platelet counts (2.1). For most symptoms reported, a large percentage of patients did not have their symptoms impact their quality of life at diagnosis.

As described by a patient: *“At the time of my diagnosis of stage 4 MCL I generally had few symptoms that made me aware that I had the disease. Only became aware as the result of a routine ultrasound.”*

As symptoms from MCL can change overtime as the disease changes, patients were asked to rate the impact of their symptoms on their current quality of life using the same rating scale. Patients rated the top symptoms causing the greatest impact to their current quality of life to be fatigue (3.3), aches and pains (2.3), and indigestion/abdominal pain/bloating (1.8) (**Table 3**).

Table 3: Symptom Impact on Patients Current Quality of Life (28 respondents)												
Symptoms	1	2	3	4	5	6	7	8	9	10	N/A	Avg Rating
Fatigue	17%	14%	4%	4%	10%	7%	4%	4%	7%	4%	25%	3.3
Aches and Pains	25%	10%	10%	4%	7%	0%	0%	4%	4%	4%	32%	2.3
Indigestion, abdominal pain, bloating	25%	3%	0%	4%	0%	4%	7%	0%	7%	0%	50%	1.8
Enlarged lymph node(s)	27%	6%	6%	3%	9%	0%	6%	0%	3%	3%	37%	1.6

Low white blood cell counts	28%	3%	4%	4%	0%	0%	0%	7%	4%	0%	50%	1.5
Low red blood cell count	28%	10%	4%	4%	0%	0%	4%	0%	4%	0%	46%	1.3

Of these MCL symptoms, patients were asked what aspects of their life were impacted. Patients stated that their symptoms most greatly impacted their ability to travel, ability to exercise, ability to concentrate, ability to perform daily activities like household chores, and ability to perform regular duties like work or volunteer.

Respondents were asked which aspects of their life, including mental and emotional problems associated with their disease, NEGATIVELY impacted their quality of life at diagnosis. All respondents (n=33) rated that one or more symptom negatively impacted their quality of life at diagnosis. Stress of diagnosis (88%), anxiety/worry (79%) and difficulty sleeping (33%) impacted patients mental and emotional well-being most at diagnosis. As years pass from a patient’s MCL diagnosis, different mental and emotional aspects related to their disease may negatively impact their quality of life. Anxiety/Worry (64%) is the top impact to a patients quality of life, followed by stress of diagnosis (46%) and Difficulty Sleeping (32%).

As described by one patient at diagnosis: *“Needed to learn a lot very quickly, and anxiety related to a lot of unknowns early on.”*

As described by one patient currently: *“I am extremely fortunate to have indolent MCL, but it can be difficult managing the anxiety of never knowing when or if I become sick and how aggressive my disease will be if I convert. It’s like living with a bomb sometimes.”*

4. Experiences With Currently Available Treatments

25 respondents provided information about their experience with MCL treatments. Following diagnosis 76% of patients required immediate treatment, while 24% remained in Watch & Wait. Of these, 29% received more than one line of treatment following MCL relapse. The most commonly reported first-line treatment (33% of respondents) was the chemoimmunotherapy regimen R-CHOP followed by stem-cell transplantation. Of those who received more than one line of treatment, treatments included BTK inhibitors such as Acalabrutinib or clinical trials. 8% of patients indicated they were dissatisfied with the number of treatments available after firstline therapy, with 36% stating they were neither satisfied or dissatisfied.

Side effects of current treatments: The most common side effects respondents experienced during their MCL treatments are listed in **Table 4**.

Side effect (n)	% of resp.	Side effect (n)	% of resp.	Side effect (n)	% of resp.
Fatigue (13)	52%	Anemia (8)	32%	Skin rash/ severe itching (5)	20%
Hair Loss (12)	48%	Neutropenia (7)	28%	Constipation (4)	16%
Thrombocytopenia (10)	40%	Confusion/Memory loss (7)	28%	Infections (4)	16%

Diarrhea (9)	35%	Mouth Sores (6)	24%	None (4)	16%
Nausea (8)	32%	Cough (5)	20%		

When asked which side effects they found most difficult to tolerate, respondents most often reported fatigue, nausea/vomiting, neurocognitive effects such as brain fog or headaches, and hair loss were the most difficult to handle (15/25 responses).

Impact of treatments on quality of life: When asked about the impact of various aspects of treatment on daily living (on a scale of 1 – 5, where 1= No impact and 5 = significant negative impact), respondents noted that treatment-related fatigue, infusion related impacts such as length of infusion and reactions, and other late side effects of treatment had the most significant impact on patients quality of life (**Table 5**).

Treatment aspect	Weighted average	Significant negative impact (rating = 4-5)	Not applicable to patient
Treatment-related Fatigue	4.5	24%	44%
Infusion Reaction	4.2	24%	40%
Infusion time	4.0	16%	40%
Late Side Effects of Treatment	4.0	16%	36%
Low Activity Level	3.9	8%	40%
Not Seeing friends/Family	3.9	20%	40%

Related to treatment access, 68% of patients did not have any difficulty accessing treatment, with 38% finding access to “not be very difficult”. The majority of patients were able to access treatment locally (76%), and only 32% of patients had to stay away from home for between 1-4 weeks to receive treatment.

Patients were asked to select all financial implications that their MCL treatment has caused. Treatment had an impact on causing patient’s to miss work (36%), and was a financial burden through drug and supplementary costs (24%) (**Table 6**).

Financial impact	% of respondents	Number of respondents
Absence from work	36%	9
None	32%	8
Drug cost	24%	6
Supplementary drug costs	24%	6
Travel	8%	2

As reported by one patient: *“I’m fortunate in that the manufacture covered the cost I needed for stem cell production. Cost of hospital parking ridiculous but our pensions are enough to cover any costs we had.”*

5. Improved Outcomes

Patient preferences: Respondents were asked to rate, on a scale of 1 -10 (1 = not important; 10 = very important), how important it is for a new MCL drug to be able to control various aspects of the patient’s disease. “Faster remission” and “allowing the patient to live longer” than current therapies were rated as the most important outcomes for a new therapy (**Table 7**).

Table 7: Treatment preferences (24 respondents)		
Treatment outcome or factor	Rating = 10 (Very important)	Weighted average
Bring about remission	100%	10
Allow me to live longer	100%	10
Control disease and symptoms associated with the disease	79%	9.3
Improve Quality of life	58%	8.54
Improve Blood Counts	58%	8.54

Respondents were asked if they would be willing to tolerate the side effects of a new treatment if they were short term. 58% (n=14) of respondents would be willing to tolerate potential side effects, while 42% were not sure. Respondents were also asked if they would choose a treatment with known side effects, potentially serious, if their doctor recommended it was the best option for them. Of the 24 respondents who answered this question, 71% selected “Yes”, while the remaining were unsure (29%).

I'm pretty much prepared to tolerate the usual side effects - nausea, fatigue, low blood counts - in order to keep living

Short term suffering for long term results is acceptable

On average patients rated the importance of having a choice in their treatment selection as 8.2 on a scale from 1 to 10 (1 being not important, 10 being extremely important). The large majority of patient’s (88%) further agree that there is a need for more effective therapy options. Patient’s listed their expectations for new treatment options:

“My great concern is that I am running out of treatment options. If I am to live, I need more options. It's really that simple.”

I would expect new therapies to be more effective than those currently available. The new therapies should give better results and better longevity than current treatments that a patient can develop resistance to in short periods of time. New therapies should offer hope to those with MCL.

Car-T therapy is the way to go - just need to improve on the implementation success rate and access. As well as reduce side effects

Experience With Drug Under Review

No Canadian patients have received this therapy through clinical trial sites, as studies were only conducted in the USA. This proved difficult to obtain patient experience on this therapy, however after thorough efforts by the LC team, one patient from the USA was able to provide their experience receiving this therapy.

The patient's demographic profile included male, aged 65-74. Prior treatment history was not provided by the patient. Access to Brexucabtagene Autoleucel (BXA) was obtained through a clinical trial.

In preparation to receive BXA, the patient was asked how prepared or knowledgeable they were regarding the different steps involved in CAR-T cell therapy before beginning. The patient was moderately prepared for steps such as the blood extraction process, wait times between extraction and infusion, possibility of required bridging therapy, and monitoring post-infusion. The patient was not prepared for numerous preparation tests involved in determining treatment eligibility.

Side effects related from treatment include neutropenia, thrombocytopenia, and anemia. The patient was not admitted to the hospital for management of these side effects and did not have these side effects last longer than 2 months post-treatment.

On a scale of 1 to 5 (1 being no negative impact, 5 being significant negative impact), the patient rated various aspects related to BXA treatment such as number of clinic visits, CAR-T extraction/infusion process, side effect monitoring and management, and travel and related costs, as a 2 on the impact to their quality of life. Using the same scale, the patient was asked about the emotional impacts of BXA treatment including worry or concern about the serious side effects and possibility of relapse. The patient rated their worry/concern over these factors as a 2 regarding its impact on their life.

For this patient, they could access treatment locally, and financial impacts included taking a short absence from work.

Based on this patient's positive experience with this treatment, they would recommend this therapy to other patients with relapsed/refractory MCL.

6. Companion Diagnostic Test

There are no companion diagnostic tests to report on for this therapy.

7. Anything Else?

Is there anything else specifically related to this drug review that CADTH reviewers or the expert committee should know?

n/a

Appendix: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH reimbursement review process, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

No

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

No

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	\$0 to 5,000	\$5,001 to 10,000	\$10,001 to 50,000	In Excess of \$50,000
Kite/Gilead				X

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

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 Date: 13-Jan-2021