CADTH

CADTH Reimbursement Review

Patient Input

CHLORMETHINE HYDROCHLORIDE (Ledaga)

(Recordati Rare Diseases Canada Inc.)

Indication: For the topical treatment of mycosis fungoides-type cutaneous T-cell lymphoma (MF-type CTCL) in adult patients.

CADTH received patient input from:

Canadian Skin Patient Alliance, Cutaneous Lymphoma Foundation, Lymphoma Canada (Joint Submission)

January 22, 2021

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Patient Input Template

Name of the Drug and Indication	**Chlormethine Hydrochloride (Ledaga) For the topical treatment of mycosis fungoides-type cutaneous T-cell lymphoma (MF-type CTCL) in adult patients.**
Name of the Patient Group	**Lymphoma Canada, Canadian Skin Patient Alliance and Cutaneous Lymphoma Foundation**
Author of the Submission	[redacted]
Name of the Primary Contact for This Submission	[redacted]
Email	[redacted]
Telephone Number	[redacted]

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

Information about the Canadian Skin Patient Alliance can be found at https://www.canadianskin.ca/en/

Information about the Cutaneous Lymphoma Foundation can be found at https://www.clfoundation.org/

2. Information Gathering

Lymphoma Canada (LC) conducted an anonymous online survey of Cutaneous Lymphoma Patients, primarily Mycosis-Fungoides patients, between September 14, 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 for lymphoma patients and survivors, physicians specializing in cutaneous lymphoma across Canada and the USA, and lymphoma organizations', primarily Cutaneous Lymphoma Foundation and the Canadian Skin Patient Alliance's own contacts. The surveys had 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 233 patients that responded to the survey, with 210 (90%) that were diagnosed with Mycosis-Fungoides (MF). Of the patients diagnosed with MF, 33% of patients (n=56) provided their experience with the Ledaga treatment for their MF, while the remainder solely provided their experience with their MF; 3% of patients were unsure if they have been treated with this product. As this treatment is available in the USA and not currently used to treat Canadian patients, experience provided on this treatment is mostly from the USA population. Of the patients who provided their demographic information (see **Tables 1 and 2),** 15% live in Canada, 56% are female, and 55% are ≥ 60 years-old.

Table 1: Country of survey respondents (233 respondents)

Respondents	CAN	USA	Europe	Other	Skipped	Total
Patients WITHOUT Ledaga experience	24	67	9	9	68	**177**
Patients WITH Ledaga experience	1	51	1	0	3	**56**

Table 2: Gender and age of survey respondents (233 respondents)

Respondents	Age Range								Gender			
	< 20	20-39	40-49	50-59	60-69	70-79	80-89	skipped	Female	Male	Prefer not to answer	Skipped
Patients WITHOUT Ledaga experience	2	12	13	23	36	19	4	68	65	42	2	68
Patients WITH Ledaga experience	0	5	4	13	15	14	2	3	26	27	0	3

3. Disease Experience

Mycosis-Fungoides (MF) can be difficult to diagnose, with symptoms that can occur for many years before a diagnosis is achieved due to different presentations of the disease. Patient's participating in this survey were for the majority diagnosed between 1-5 years ago (44%), with a portion of patients diagnosed over 10 years ago (20%). Patients were asked whether their MF was misdiagnosed as another skin condition before it was later diagnosed as MF. Only 25% of patients had their condition correctly diagnosed as MF at presentation. The remainder of patients received diagnoses of eczema (36%), dermatitis (26%), psoriasis (18%) and allergic reaction (10%), among others. As two patients described:

"I went to three doctors and then the fourth doctor found the mycosis fungoides diagnosis."

"After 7 years of misdiagnosis, I was correctly diagnosed"

MF symptoms that most impacted affected patients' quality of life at diagnosis (196 respondents) included visual patches or lesions (raised, scaly or discolored) (86%), itchiness of skin or lesions (56%),

pain or burning of skin or lesions (32%), visual appearance of thick raised lesions (plaques) (30%), and visual appearance of rash-like skin redness over the entire body (22%).

Respondents were asked which aspects of their life, including mental and emotional problems, were NEGATIVELY impacted by their MF symptoms at diagnosis. The majority of respondents (94%) had one or more symptom negatively impact their quality of life **(Table 3).**

Table 3: Impact of MF-CTCL on patients' mental and emotional well-being (104 respondents)		
	# of respondents	**% of respondents**
Stress of Diagnosis	146	74%
Anxiety/Worry	134	68%
Concerns of body image/physical appearance changes	85	43%
Difficulty Sleeping	70	35%
Self-conscious/embarrassment	68	34%
Depression	51	26%
Problems concentrating	46	23%
Financial concerns	45	23%

Patients were asked about their current symptoms and impacts to their quality of life and wellbeing, as a change in disease and its impacts may have occurred since diagnosis. 43% of patients did not have their MF progress, while the majority did have their MF progress with 30% of patients having patches cover more of their body and 13% with increases in their patches or raised/plaques. Symptoms that most commonly affected respondents' quality of life currently (196 respondents) are similar to those at diagnosis, and include visual appearance of skin patches or lesions (58%), itchiness of skin or lesions (47%) and pain or burning of skin or lesions (22%). Current wellbeing of patients has been impacted by anxiety/worry (51%), stress of diagnosis (39%), and concerns about body image/physical appearance changes (33%). Patients found that living with MF has impacted their personal image (43%), family (33%), intimate relations (28%), and work (24%). 38% of patients did not have their life affected in these areas. Patients have reported:

"I can manage obligations but not without detailed, planned coordination. However, when an itch flare-up occurs, my favorite activities such as running are very uncomfortable."

"Now that Covid-19 has introduced us all to social distancing, isolation, face-mask wearing and avoidance of public events, I feel as if the world has gotten a taste of my world post-diagnosis. For 7 years I have had to be on "lockdown" and restrict my public, leisure and work involvements."

"I worry that if my MF progresses beyond stage 1 that my common-law relationship will not last. Trying to apply the cortisone cream by myself is difficult as I can't always see when new patches are coming out. Afraid to ask for help when home to apply the cream for fear of rejection or argument."

"Prior to treatment the redness and scaly patches made me self-conscious of the appearance of my skin, especially when the disease progress to areas that were visible in summer clothes."

4. Experiences With Currently Available Treatments

171 respondents provided information about their experience with MF-CTCL treatments. As there are many treatment options including systemic therapies, radiation treatment, light therapy and topical agents for patients, the top treatment options in each category have been summarized in **Table 4**.

Table 4: Treatments for Patients with MF-CTCL (171 respondents)							
Topical Drug Treatment	**% of Respondents**	**Light Treatment**	**% of Respondents**	**Systemic Treatment**	**% of Respondents**	**Radiation Treatment**	**% of Respondents**
Topical steroids	89%	**UVB light therapy**	49%	**No systemic treatment**	56%	**No Radiation treatment**	71%
Retinoids	26%	**No phototherapy treatment**	27%	**Methotrexate**	18%	**Local radiation**	21%
Compounded nitrogen mustard	26%	**UVA light therapy**	20%	**Bexarotene**	17%	**Total skin electron beam**	11%
Other	24%	**PUVA light therapy**	16%	**Other**	16%		

Side effects of current treatments: The most common side effects respondents experienced by patients during their MF-CTCL treatments are listed in **Table 5**.

Table 5: Side effects from treatment (171 respondents)					
Side effect (n)	**% of resp.**	**Side effect (n)**	**% of resp.**	**Side effect (n)**	**% of resp.**
Fatigue (72)	42%	Skin discoloration (51)	30%	None	19%
Itchiness (69)	40%	Hair loss (39)	23%	Nausea (27)	16%
Skin irritation or rash (64)	37%	Other (39)	23%	Peripheral Neuropathy (23)	13%
Skin pain or burning (59)	35%	Skin rashes/ severe itching (33)	19%	Infections (20)	12%

Respondents found fatigue, hair loss, severe itchiness, and skin burning and pain, to be the most difficult to tolerate side effects of treatment for their MF (92 respondents).

Impact of treatments on quality of life: When asked about the impact of various aspects of treatment on their daily living (on a scale of 1 – 5, where 1= No impact and 5 = significant negative impact), respondents noted that the number of clinic visits and treatment-related fatigue had the most significant impact on their quality of life **(Table 6).**

Table 6: Impact of treatment on quality of life (171 respondents)		
Treatment aspect	**Weighted average**	**Significant negative impact (rating = 4-5)**

# of clinic visits	2.6	30%
Treatment related fatigue	2.6	27%
Length of time for treatment administration	2.4	23%
Side Effects of treatment	2.3	22%
# of infections	1.8	11%

Patients were asked which areas of their life were negatively impacted by their treatments, using a similar rating scale as above. Patients rated activities (2.5), work (2.4), and travel (2.4), to be negatively impacted by their treatment. As alluded by one patient: *"I cannot travel long periods of time or even live far away from the treatment clinic."*

Access to treatment within the patients community is an important consideration. 33% of patients had difficulty accessing treatment locally, resulting in long travel times that can impact patients' quality of life (171 respondents). As reported by two patients on their experience accessing treatment:

"[hospital] isn't close, but I prefer going there than a local place with no specialist. Traveling there takes time and a lot of money in tolls and parking fees."

"One hour travel required for treatment. Number of treating facilities seems limited. Have traveled as far as 100 miles one way for treatment."

Patients were asked about the financial impact that treatment has had. Out-of-pocket costs and costs related to treatment resulted in the greatest financial impact to patients **(Table 7)**.

Table 7: Financial implications of treatment for MF patients (171 respondents)

Financial impact	Weighted Average	Significant negative impact (rating = 4-5)
Out of Pocket Costs	2.5	25%
Cost of treatment	2.3	20%
Time off work	2.2	14%
Travel for Treatment	2.1	14%
Supplemental drug costs	2.0	13%

5. Improved Outcomes

Patient's were asked whether there were enough treatment options available to them to manage/treat their MF. 16% of patients do not have enough treatment options available to them. Though the majority state they do have access to enough treatment options, most patients responding to this survey are within the USA where there are more treatment options approved for use. Further, 81% of patients indicate it is extremely important for both themselves and their clinician to have choices in different treatment approaches (171 respondents). According to one patient: *"I am always on the quest for more and better treatment options that will improve my overall quality of life and health."*

Patient preferences: Respondents were asked to rate, on a scale of 1 -5 (1 = not important; 5 = extremely important), the importance of various factors regarding a new drug or therapy for MF-CTCL. "Longer survival" and "better quality of life" compared to current therapies were rated as the most important outcomes for a new therapy to address **(Table 8).**

Table 8: Treatment preferences (171 respondents)		
Treatment outcome or factor	**Rating = 5 (Extremely important)**	**Weighted average**
Longer survival	83%	4.7
Better quality of life	71%	4.5
Longer Remission	66%	4.5
Fewer side effects	51%	4.1
Easier/Faster Treatment Application	46%	4.0

Respondents were asked if they would be willing to tolerate the side effects of a new treatment if they were short term. 37% (n=64) of respondents would be willing to tolerate potential side effects, while 13% were not; the remaining were unsure (50%) for reasons depending on the type of side effect, duration, and cost-benefit ratio. 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 171 respondents who answered this question, 28% selected "Yes", while only 13% selected "No"; the remainder were unsure for similar reasons above. Current gaps in accessing treatment according to patients included lack of resources and difficulties in accessing treatments:

"My only treatment gap related to Valchlor as I was unable to get it in Canada. I needed to travel to the US to purchase it!"

"Phototherapy due to covid virus hospital shut down"

"Health care providers should advocate for better policies and supports for patients to be protected against workplace discrimination or being mysteriously let go while in treatment. There should also be more health care available outside of working hours to avoid pressures and strain on employment. Mental health services should be covered and patients should be referred when they are diagnosed, not years later when they hear about support organizations on their own."

"More resources for information, support and advocacy required for this rare disease in Canada"

6. Experience With Drug Under Review

56 patients (33% of respondents) received treatment with Ledaga. Patients largely accessed this treatment through private insurance (52%), while 19% of patients accessed through patient support programs such as compassionate access from the drug manufacturer. 56% of patients were receiving another treatment at the same time they were using Ledaga, including options such as light therapy, systemic therapies, and radiation treatment.

Side Effects: 13% of patients were able to complete their full course of Ledaga, while 30% are currently still receiving this treatment; 20% of patients had to stop this treatment due to side effects, while the other 20% did not have their symptoms controlled by this therapy (54 respondents). Ledaga was able to manage patient's MF symptoms including red skin patches (56%), skin itchiness (31%), skin ulcers (15%), and skin pain (15%). The most commonly reported side effects of Ledaga treatment included itching

(37%), hyperpigmentation (33%), skin blistering (26%), rash (24%), or no symptoms (24%). As reported by two patients:

"This treatment does work, although some individuals may experience reactions to the skin, and should be careful while using it."

"Even though it caused a reaction to my skin, which caused me to leave the trial early, it did clear all of the MF areas that were being treated."

Quality of Life: 54 respondents provided details on whether their quality of life was impacted by various aspects of the treatment, rating this impact on a scale of 1 (no negative impact on my life) to 5 (significant negative impact on my life). None of the weighted averages for these responses was higher than 3, suggesting that Ledaga did not have a significant negative impact on patients' quality-of-life **(Table 9).**

Table 9: Impact of Ledaga therapy on patients Quality of Life (54 respondents)

Aspect of Ledaga therapy	Weighted average	Rating 1-2 (Minimal Negative Impact (%)	Rating 4-5 (Significant Negative Impact) (%)
Treatment-related side effects	2.7	46%	26%
Frequency of Application	2.4	61%	28%
Length of time to dry	2.4	57%	24%
Length of time to apply	2.0	73%	18%
# of Infections	1.7	57%	9%

When asked about which aspects of their life were impacted by Ledaga treatment and side effects, the majority of patients rated that Ledaga did impact patients ability to exercise, work/volunteer, spend time with family/friends, and fulfill daily obligations and activities (i.e household chores, etc.). 20% of patients did have difficulties with travel, largely because Ledaga needed to remain refrigerated. The majority of patients did not have any negative financial impacts caused by Ledaga through time off work and medication to manage side effects. However, 20% of patients were negatively impacted financially due to the cost of this treatment.

When asked how Ledaga treatment improved their overall health and well-being, 32% of patients indicated it was somewhat improved, with 19% stating it is greatly improved; 39% of patients were unchanged (54 respondents). One patient commented:

"It was the only treatment that efficiently dealt with my stubborn patches/plaques. Had it not been effective, my treatment was going to be with IV chemotherapy with known significant side effects. I feel that managing my disease with Ledaga literally saved my life."

Overall Experience and Recommendation Ledaga Therapy: When asked to describe their experience with Ledaga, 46% of patients responded they had a good to excellent experience with the therapy, and 74% of patients mentioned they would take this treatment option again if available to them. Patients further commented:

"Ledaga has maintained the positive effect originally delivered from my PUVA treatment. I have been very stable, neither positive or negative reactions."

"It is the only treatment I have had that has improved my skin at all."

"Other than cost and difficulty to get in Canada, it was a game changer for me."

7. Companion Diagnostic Test

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

8. Anything Else? 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.

   Yes. Susan Thornton from the Cutaneous Lymphoma Foundation (CLF) and Rachael Manion from the Canadian Skin Patient Alliance (CSPA) both contributed to survey development, outreach to cutaneous lymphoma patients globally, and reviewed and provided feedback on the final report prior to submission.

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.

   n/a

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
n/a				

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.

Name: Kaitlyn Beyfuss-Laski
Position: Manager of Patient Programs, Research & Advocacy
Patient Group: Lymphoma Canada
Date: 14-Jan-2021

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The Canadian Skin Patient Alliance (CSPA) worked with Lymphoma Canada and the Cutaneous Lymphoma Foundation to develop the survey and submission.

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N/A				

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Name: Rachael Manion
Position: Executive Director
Patient Group: Canadian Skin Patient Alliance
Date: January 25, 2021

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Recordati	X			
Helsinn				X

4.

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.

Name: Susan Thornton
Position: CEO
Patient Group: Cutaneous Lymphoma Foundation
Date: January 25, 2021