Canada's Drug Agency
L'Agence des médicaments du Canada

CDA-AMC REIMBURSEMENT REVIEW

Patient and Clinician Group Input

asciminib (Scemblix)

(Novartis Pharmaceuticals Canada Inc.)

Indication: For the treatment of adult patients with newly diagnosed or previously treated Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP).

March 24, 2025

This document compiles the input submitted by patient groups and clinician groups for the file under review. The information is used by CDA-AMC in all phases of the review, including the appraisal of evidence and interpretation of the results. The input submitted for each review is also included in the briefing materials that are sent to expert committee members prior to committee meetings. **If your group has submitted input that is not reflected within this document, please contact Formulary-Support@cda-amc.ca.**

Disclaimer: The views expressed in this submission are those of the submitting organization or individual. As such, they are independent of CDA-AMC and do not necessarily represent or reflect the views of CDA-AMC. No endorsement by CDA-AMC is intended or should be inferred.

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Patient Input Template

Name of the Drug and Indication	Asciminib
Name of the Patient Group	Heal Canada
Author of the Submission	Brigitte Leonard, Ph.D

About Your Patient Group

Heal Canada is a registered not-for-profit organization that aims to empower patients, improve healthcare outcomes, and advocate for equitable access to quality healthcare across Canada. We are committed to fostering a patient-centered healthcare system that prioritizes every individual's well-being, dignity, and rights through:

- Patient Empowerment
- Patient Education and Awareness
- Advocacy for Equity
- Collaboration and Partnerships with the highest ethical standards.

Website: https://healcanada.org

Information Gathering/ Methodology

- Patient Survey
    - Canadian: 15 patients
    - Total Participants: 15 patients
- Patient on asciminib interview
    - 16 non-Canadian

Disease Experience

- In Canada, 40% are diagnosed within a week, 40% within three months and 20% after three months
- -Their understanding of the test requirements was good.
- Their understanding of the treatment was good.

- -Most patients were asymptomatic before diagnosis and had relatively good overall health and QoL.
- -Treatment impact significantly affects their QoL and working capability. Taking a pill for the rest of their life is not something they tend to appreciate. They wish to be able to stop and remain in remission.

Experiences With Currently Available Treatments

- Most survey patients are treated with Imatinib for more than 5 years. No participant was on asciminib.
- Most patients didn't experience treatment delays. However, some patients can experience delays at the pharmacy due to a lack of stock.
- 80% of patients experienced a decline in overall health, all attributed to treatment side effects.
- Eighty percent of participants experience fatigue, pain, sleep issues, and reduced daily living and functional capabilities (Table 1).

Table 1: Side effects experienced with the current medication

Symptoms	Frequency
Fatigue	100%
Pain	80%
Sleep issues	80%
Reduced daily living and functional capabilities.	80%
Emotional and mental health issues.	60%
Reduced social relationships and support.	40%
Reduced sexuality and negative impact on body image	40%
Impacted cognitive functioning: spirituality and meaning.	40%
Depression or Anxiety due to fears and future perspectives	20%

- The treatment side effects impacted the financial situation of 80% of participants. They have an average concern about their finances of 73.7%, where 100% are very concerned.
- 60% of participants adhere to a long-term disablement program due to side effects.

- Some participants lost their employment, too.
- Some retired earlier than anticipated.
- Their current medication impacts their QoL with an average of 73.6%, with 100 being severely affected.
- Fatigue and pain are mentioned in several cases as the reason for frequent challenges observed: poor QoL (100%, financial struggles (80%), poor mental health (60%), reduced social activities (80%), and difficulty managing family responsibilities (60%).

Treatment-free remission: the best solution for patients and payers

Initially, physicians were prescribing TKI to CML patients until the patient ceased to respond or died. The medical community thought that TKIs couldn't cure CML patients like transplantation. Less than a decade after the approval of imatinib and with the sophistication of the monitoring technique, Dr. Mahon's team demonstrated that some patients who reached undetectable levels of BCR-ABL cells could stop their treatment and remain in remission.[1] Over time, the CML expert community named the treatment-free remission (TFR) phenomenon, refusing to use the term cure because roughly half of the patients needed to reinitiate their treatment due to a return of BCR-ABL cells to detectable levels.

The depth of response is the principal factor in attempting a supervised treatment discontinuation. Most TKIs have been studied in the context of TFR, and successful TFR is possible with all of them as long as the disease is below 4 or 4.5 logs of detection, called deep molecular response (DMR) or MR4 or MR4.5.[2]Asciminib is not an exception; sustained TFR is achievable.[3]

Initially, the medical community thought that only a minority of patients could attempt TFR. These patients needed to respond well in their first line, reach DMR and maintain their treatment for an extended period without a resurgence of bcr-abl cells. The current recommendation for attempting TFR is 6 to 10 years. However, most patients enrolled in these trials were treated with imatinib. Clinical trials with more potent TKIs, such as nilotinib, have demonstrated similar results with a much shorter treatment period duration needed (ENESTfreedom).[4]

Several clinical studies have demonstrated that healthcare professionals (HCPs) can safely attempt TFR in patients who receive several lines of therapy as long as they achieve DMR. ENESTop, DASfree, DADI and EURO-SKI, to name a few.[2]

At ASH 2024, additional real-world studies add to the evidence that patients can safely attempt TFR in various contexts:

- Patients who failed several lines of treatment.[5]
- Patients with additional mutations such as ASXL1.[6]
- Patients in lower-income countries or cities.[7]

Imatinib is not the best TKI for patients who want to attempt TFR. The choice of the 1st line can significantly impact patients' chances of reaching TFR and the duration of treatments. Fewer patients reached DMR when treated with imatinib versus second-generation TKIs (30% vs 50%). Also, patients treated with second-generation TKIs can stop earlier because they achieve DMR faster. Some early responders can stop after only three years of treatment. Asciminib, the most recent TKI, provides a quicker and more profound response than second-generation TKIs, making it the best 1st line option to maximize patients' opportunity to attempt TFR as fast as possible.

Why does Asciminib seem to be the best front-line treatment?

Regardless of the possibility of TFR, the choice of front-line TKI is crucial for patient outcomes. It impacts the patient's odds of acquiring additional mutations and progressing to more aggressive forms. Progression is a death sentence for most patients with a survival rate inferior to a year.

Most patients respond well to all TKIs; 5% or less will progress to a more aggressive phase if they take their medication as prescribed. So, choosing one TKI over another does not impact survival curves. However, progressions tend to occur quickly in the first months of treatment. The level of response to a TKI at 3 months predicts patients' survival chances, and even if a switch of TKIs is done, it cannot always change the patient's fate.

In fact, Dr. David Marin has published research on the predictive value of the 3-month BCR-ABL1 transcript levels in patients with chronic myeloid leukemia (CML) treated with tyrosine kinase inhibitors (TKIs). In a study involving 282 patients, Dr.

Marin and colleagues found that BCR-ABL1 transcript levels at 3 months post-treatment initiation were significant predictors of long-term outcomes, including overall survival (OS), progression-free survival (PFS), complete cytogenetic response (CCyR), major molecular response (MMR), and complete molecular response (CMR). Patients with transcript levels above 9.84% at 3 months had markedly lower 8-year probabilities of OS and CCyR than those with lower levels.

When we analyzed phase III trials conducted in a front-line setting, we saw a clear trend: at least two times more patients in the imatinib group (2-5%) progressed during the first year compared to the second-generation TKIs and asciminib (1-2.3%).[9,10,11]

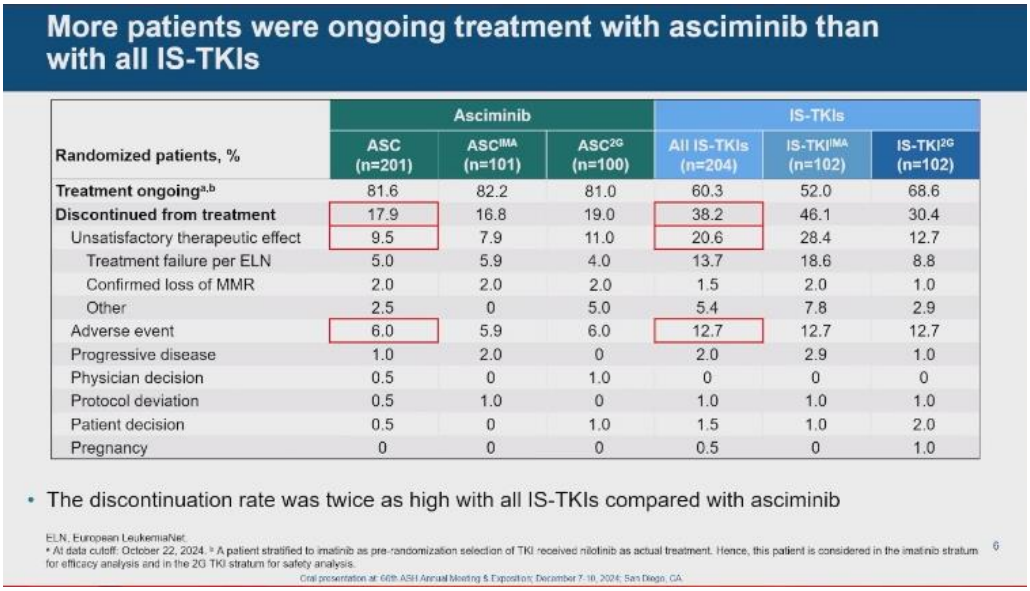
Based on several registries and real-world studies at ASH, imatinib remains the most prescribed TKI in the front-line setting. Why do patients continue to receive an inferior TKI? Imatinib has a perceived better cardiovascular (CV) safety profile. The medical community recommends avoiding second-generation TKIs in patients with CV risk factors regardless of the severity of CML.

To assess the impact of these recommendations, Dr. Kim's team at Princess Margaret Toronto analyzed CML outcomes in line with a validated CV risk score (Framingham Risk Score).[12] At diagnosis, 40 to 60% of CML patients have at least one comorbid condition, and 30% present with CV risk factors. Patients with CV risk factors tend to receive imatinib more than patients without risk (69.2% vs. 14.9%). In this analysis, the type of front-line TKI is the most critical factor influencing treatment outcomes, with second-generation TKIs showing superior results to imatinib. These results highlight the need for alternative treatments with better efficacy and tolerability.

Asciminib emerges as a promising 1st line option for CML patients. The ASC4FIRST Study's 96-week follow-up has revealed that asciminib provides a superior response rate and boasts a better-tolerated profile in the front line compared to all other TKIs (imatinib and second-generation TKIs). This exciting development paves the way for a more effective and tolerable CML treatment.

On asciminib, two times fewer patients discontinued treatment due to unsatisfactory therapeutic effects or adverse effects (Figure 1).[11]

Figure 1: Patient Disposition Slide Presented at ASH 2024[11]



More patients were ongoing treatment with asciminib than with all IS-TKIs

Randomized patients, %	Asciminib			IS-TKIs		
	ASC (n=201)	ASC^{IMA} (n=101)	ASC^{2G} (n=100)	All IS-TKIs (n=204)	IS-TKI^{IMA} (n=102)	IS-TKI^{2G} (n=102)
Treatment ongoing[a,b]	81.6	82.2	81.0	60.3	52.0	68.6
Discontinued from treatment	17.9	16.8	19.0	38.2	46.1	30.4
Unsatisfactory therapeutic effect	9.5	7.9	11.0	20.6	28.4	12.7
Treatment failure per ELN	5.0	5.9	4.0	13.7	18.6	8.8
Confirmed loss of MMR	2.0	2.0	2.0	1.5	2.0	1.0
Other	2.5	0	5.0	5.4	7.8	2.9
Adverse event	6.0	5.9	6.0	12.7	12.7	12.7
Progressive disease	1.0	2.0	0	2.0	2.9	1.0
Physician decision	0.5	0	1.0	0	0	0
Protocol deviation	0.5	1.0	0	1.0	1.0	1.0
Patient decision	0.5	0	1.0	1.5	1.0	2.0
Pregnancy	0	0	0	0.5	0	1.0

- The discontinuation rate was twice as high with all IS-TKIs compared with asciminib

ELN, European LeukemiaNet.
[a] At data cutoff: October 22, 2024. [b] A patient stratified to imatinib as pre-randomization selection of TKI received nilotinib as actual treatment. Hence, this patient is considered in the imatinib stratum for efficacy analysis and in the 2G TKI stratum for safety analysis.

Oral presentation at: 66th ASH Annual Meeting & Exposition; December 7-10, 2024; San Diego, CA.

On asciminib, more patients reach DMR and can attempt TFR (Figure 2).[11] In less than 2 years of treatment, 50% of patients can start a consolidation phase before attempting TFR (Figure 3). In general, asciminib provides a better response rate than the second generation and less discontinuation due to adverse events.

Figure 2: Depth of Molecular Response Slide Presented at ASH 2024[11]

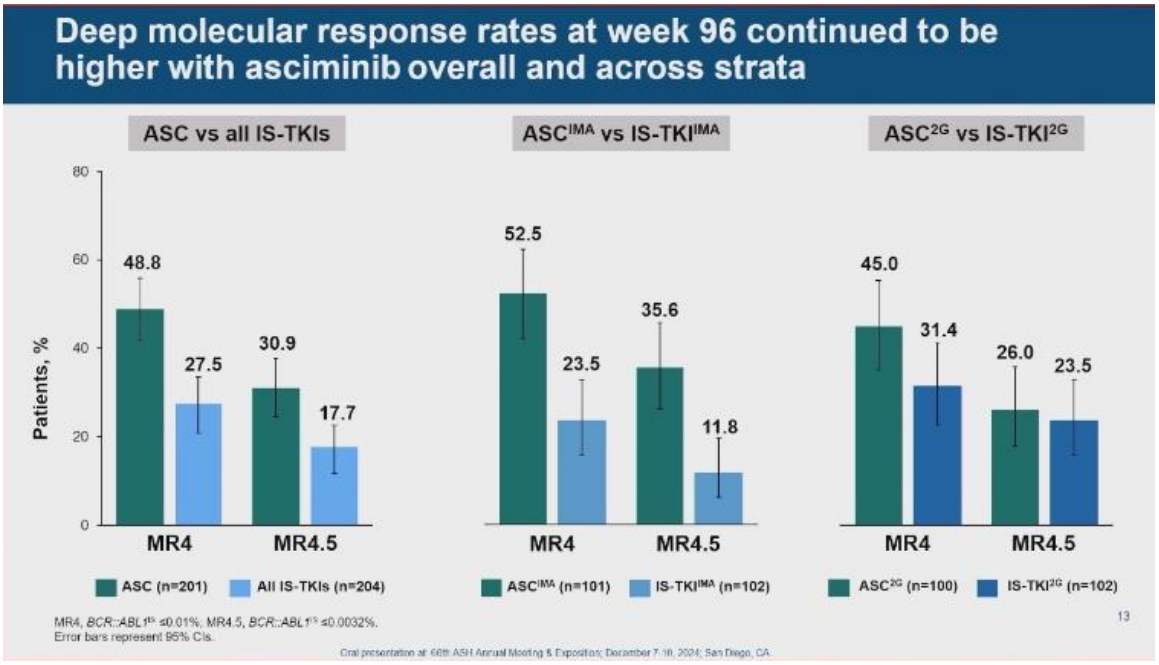
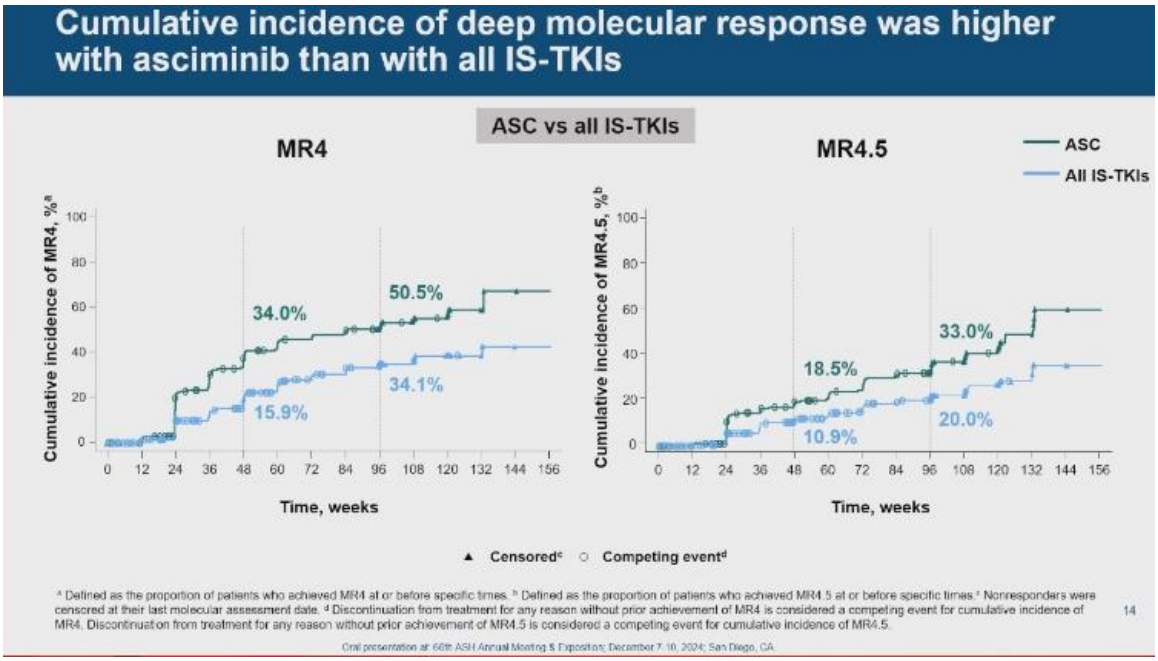


Figure 3: Cumulative Depth of Molecular Response Slide Presented at ASH 2024[11]



Experience With Drug Under Review

Most people had access to asciminib in TKI failure. Of 16 interviews, only three patients failed asciminib after several treatment lines, representing an 81% success rate.

Adverse effects experienced with asciminib tend to be less than other TKI. Several persons mentioned experienced any side effects. Most side effects mentioned are joint pain, fatigue, skin rash and brain fog. People who switch to asciminib from other TKI tend to be optimistic regarding the tolerability profile of asciminib:

"After the side effects of Gleevec and Bosulif, Scemblix has been wonderful compared to the other two."

"I honestly had a lot of pain, muscle and joint pain mostly. I started on 80mg, dropped to 40, couldn't tolerate it, I'm ok 20 now and still maintain DMR."

"I had side effects with other TKI's, and I am very grateful to Scemblix"

Companion Diagnostic Test

Asciminib does not require additional testing compared to other TKIs used in CML.

Anything Else?

In conclusion, with asciminib in the first line, TFR will be an option for more patients and significantly shorten the treatment duration; a shorter treatment duration means a lower treatment cost per patient, including a shorter TKI intake and fewer adverse reaction management costs.

Fewer patients will have to switch to the second and third lines of treatment or receive transplantation, which can be costly, healthcare resource intensive and less efficient.

Reference

1- Mahon FX et al, Discontinuation of imatinib in patients with chronic myeloid leukaemia who have maintained complete molecular remission for at least 2 years: the prospective, multicentre Stop Imatinib (STIM) trial, Lancet Oncol, 2010 Nov;11(11):1029-35
2- Bourne G. et al., Treatment-Free Remission in Chronic Myeloid Leukemia, J. Clin. Med. 2024, 13, 2567.
3- Yousefi. A et al, Sustained treatment-free remission in two chronic myeloid leukemia patients after asciminib discontinuation: a report of two cases, Ann Hemato, 2025 Jan 10.
4- Hochhaus A et al. Treatment-free remission following frontline nilotinib in patients with chronic myeloid leukemia in chronic phase: results from the ENESTfreedom study, Leukemia . 2017 Jul;31(7):1525-1531.
5- Rebechi M et al, Comparison of Long-Term Outcomes Among Patients with Chronic Myeloid Leukemia Who Undergo Initial Tyrosine Kinase Inhibitor Dose Reduction Versus Tyrosine Kinase Inhibitor Switch, ASH 2024, Abstract 1771
6- *Soverini et al.* ASXL1 Mutations at Diagnosis Did Not Impact on the Depth of Molecular Response (MR) and on Treatment-Free Remission (TFR) Eligibility in Chronic Phase (CP) Chronic Myeloid Leukemia (CML) Patients (pts) Receiving either Nilotinib (NIL) First-Line or Imatinib (IM) with Early Switch to NIL in Case of No Optimal Response in the SUSTRENIM Clinical Trial, Abstract 3158
7- *Bonuomo et al.,* Tyrosine Kinase Inhibitors Discontinuation in Chronic Myeloid Leukemia: Observational Study of 673 Patients in Italy, Abstract 3162
8- *Marin D et al,* Assessment of BCR-ABL1 transcript levels at 3 months is the only requirement for predicting outcome for patients with chronic myeloid

leukemia treated with tyrosine kinase inhibitors, J Clin Oncol. 2012 Jan 20;30(3):232-8.
9- Saglio G. et al, Nilotinib versus imatinib for newly diagnosed chronic myeloid leukemia, N Engl J Med. 2010 Jun 17;362(24):2251-9.
10- Kantarjian et al, Dasatinib or imatinib in newly diagnosed chronic-phase chronic myeloid leukemia: 2-year follow-up from a randomized phase 3 trial (DASISION), Blood. 2012 Feb 2;119(5):1123-9.
11- Cortes et al. ,Asciminib (ASC) Demonstrates Favorable Safety and Tolerability Compared with Each Investigator-Selected Tyrosine Kinase Inhibitor (IS TKI) in Newly Diagnosed Chronic Myeloid Leukemia in Chronic Phase (CML-CP) in the Pivotal Phase 3 ASC4FIRST Study, abstract 475
12- Chiu M. et al,Prognostic Implication of Framingham Risk Score As a Comorbidity Measure on Treatment Outcomes Following First-Line Tyrosine Kinase Inhibitor in Newly Diagnosed CML Patients, abstract 1768

Appendix: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the 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. CDA-AMC may contact your group with further questions, as needed.

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

No

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

No

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
Novartis Canada			X	
SOBI USA				X
GSK Canada			X	
Servier Canada			X	
Daiichi-Sankyo Canada			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.

Name: Brigitte Leonard

Position: Chief Scientific Officer

Patient Group: Heal Canada

Date: 23-03-2025

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Drugs. Health Technologies and Systems. Médicaments, technologies de la santé et systèmes.

Patient Input Template

Name of the Drug and Indication	**Scemblix (Ascinimib)**
Name of the Patient Group	**The Chronic Myelogenous Leukemia Society of Canada**
Author of the Submission	**Cheryl-Anne Simoneau**

1. About Your Patient Group

Describe the purpose of your organization. Include a link to your website.

Answer: **The Chronic Myelogenous Leukemia Society of Canada is dedicated to supporting patients with Chronic Myeloid Leukemia (CML) through education, advocacy, and research. Our mission is to improve the quality of life for CML patients and their families. More information can be found on our website: www.cmlsociety.org**

2. Information Gathering

Canada's Drug Agency (CDA-AMC) is interested in hearing from a wide range of patients and caregivers in this patient input submission. Describe how you gathered the perspectives: for example, by interviews, focus groups, or survey; personal experience; or a combination of these. Where possible, include **when** the data were gathered; if data were gathered **in Canada** or elsewhere; demographics of the respondents; and **how many** patients, caregivers, and individuals with experience with the drug in review contributed insights. We will use this background to better understand the context of the perspectives shared.

Answer: **We gathered perspectives through a pulse survey conducted among CML patients who have been treated with Scemblix. The survey included responses from patients in Canada (Quebec, Ontario, British Columbia), the United States, and other countries (U.K. , France). Data was collected from January 2024 to March 2025, involving over 20 patients who shared their experiences with Scemblix. Additionally we conducted phone interviews for local patients.**

3. Disease Experience

CDA-AMC involves clinical experts in every review to explain disease progression and treatment goals. Here we are interested in understanding the illness from a patient's perspective. Describe how the disease impacts patients' and caregivers' day-to-day life and quality of life. Are there any aspects of the illness that are more important to control than others?

Answer: **CML significantly impacts patients' daily lives and quality of life. Patients often experience fatigue, pain, and emotional stress, which can affect their ability to work, socialize, and perform daily activities. Since a majority of patient must stay on the drugs for most of their normal life spans, it is important to have options for patients. Long-term use of any specific drug can cause different experiences of side effects that increase with toxicity over time. It is essential for these patients to have alternative drug treatments, if they cannot be**

considered for Treatment Free Remission trials. Controlling symptoms such as fatigue and maintaining a good quality of life are crucial for patients, as it helps patient to be compliant with treatments and ensure that the treatment is taken consistently.

4. Experiences With Currently Available Treatments

CDA-AMC examines the clinical benefit and cost-effectiveness of new drugs compared with currently available treatments. We can use this information to evaluate how well the drug under review might address gaps if current therapies fall short for patients and caregivers.

Describe how well patients and caregivers are managing their illnesses with currently available treatments (please specify treatments). Consider benefits seen, and side effects experienced and their management. Also consider any difficulties accessing treatment (cost, travel to clinic, time off work) and receiving treatment (swallowing pills, infusion lines).

Answer: Patients have used various TKIs, including Imatinib, Dasatinib, and Bosulif, before starting Scemblix. While these treatments have been effective for some, many patients experienced significant side effects such as fatigue, muscle pain, and gastrointestinal issues. In some cases other treatment has addressed the needs quite well, but due to the long term nature of treatment for this specific disease, it can happen that patients experience a buildup of side effects that increase in toxicity over time. Therefor switching treatments brings welcomed relief for these patients and allows them to continue on uninterrupted treatment. Access to treatment can also be challenging due to costs in provinces other than Manitoba, Saskatchewan, Alberta and B.C. in these provinces, the cost of the treatment is included with the provincial cancer care centres. Whereas patient who live in Ontario, Quebec, New Brunswick, Nova Scotia, P.E.I. and Newfoundland, must access their provincial reimbursement programs and/or access employer drug benefit plans. In some cases, non-geographic patients experience difficulty in accessing their healthcare teams when it comes to the need for frequent monitoring.

5. Improved Outcomes

CDA-AMC is interested in patients' views on what outcomes we should consider when evaluating new therapies. What improvements would patients and caregivers like to see in a new treatment that is not achieved in currently available treatments? How might daily life and quality of life for patients, caregivers, and families be different if the new treatment provided those desired improvements? What trade-offs do patients, families, and caregivers consider when choosing therapy?

Answer: Patients and caregivers desire treatments that offer better symptom control, fewer side effects, and improved quality of life. A new treatment that provides these improvements would significantly enhance daily life and reduce the emotional and physical burden on patients and their families. Patients are willing to trade off some side effects for a treatment that offers better overall management of their condition.

6. Experience With Drug Under Review

CDA-AMC will carefully review the relevant scientific literature and clinical studies. We would like to hear from patients about their individual experiences with the new drug. This can help reviewers better understand how the drug under review meets the needs and preferences of patients, caregivers, and families.

How did patients have access to the drug under review (for example, clinical trials, private insurance)? Compared to any previous therapies patients have used, what were the benefits experienced? What were the disadvantages? How did the benefits and disadvantages impact the lives of patients, caregivers, and families? Consider side effects and if they were tolerated or how they were managed. Was the drug easier to use than previous therapies? If so, how? Are there subgroups of patients within this disease state for whom this drug is particularly helpful? In what ways? If applicable, please provide the sequencing of therapies that patients would have used prior to and after in relation to the new drug under review. Please also include a summary statement of the key values that are important to patients and caregivers with respect to the drug under review.

Answer: Patients accessed Scemblix through clinical trials and private insurance. Compared to previous therapies, Scemblix provided better blood counts, reduced fatigue, and improved quality of life. Side effects were generally less severe than those experienced with other TKIs. Patients found Scemblix easier to use, with fewer disruptions to their daily lives. Subgroups of patients who were intolerant or resistant to other TKIs found Scemblix particularly beneficial. The benefits included improved results, the treatment more effectively targeted the oncogene causing the disease. In cases where patients had developed additional mutations/resistance to the other drug, Scemblix, due to its enhanced ability to target a broader spectrum of mutations, significantly improved patients chances of achieving deep molecular responses that not only extend their chances of survival, as well as improve their quality of life.

7. Companion Diagnostic Test

If the drug in review has a companion diagnostic, please comment. Companion diagnostics are laboratory tests that provide information essential for the safe and effective use of particular therapeutic drugs. They work by detecting specific biomarkers that predict more favourable responses to certain drugs. In practice, companion diagnostics can identify patients who are likely to benefit or experience harms from particular therapies, or monitor clinical responses to optimally guide treatment adjustments.

What are patient and caregiver experiences with the biomarker testing (companion diagnostic) associated with regarding the drug under review?

Consider:

- Access to testing: for example, proximity to testing facility, availability of appointment.

- Testing: for example, how was the test done? Did testing delay the treatment from beginning? Were there any adverse effects associated with testing?
- Cost of testing: Who paid for testing? If the cost was out of pocket, what was the impact of having to pay? Were there travel costs involved?
- How patients and caregivers feel about testing: for example, understanding why the test happened, coping with anxiety while waiting for the test result, uncertainty about making a decision given the test result.

Answer: There is no specific companion diagnostic test associated with Scemblix, specifically. However, as with all CML patients, regular monitoring of blood counts and molecular response testing through Polymer Chain Reaction (PCR) that can detect the presence of the BCR ABL transcripts (oncogene) which is the specified marker of this targeted therapy and is the known harbinger of the disease, is essential to assess the effectiveness of the treatment. Patients generally understand the importance of these tests and cope well with the associated anxiety and uncertainty. This testing has been well established and is in fact the treatment protocol for CML. The cost for the testing is included in Canadian universal healthcare and done in hospital during the appointment with the treating hematologist/oncologist.

8. Anything Else?

Is there anything else specifically related to this drug review that CDA-AMC should know?

Answer: Scemblix has shown significant potential as a frontline therapy for CML. Patients have reported substantial improvements in their quality of life and overall treatment experience. We strongly recommend that Scemblix be considered for approval as a frontline therapy for CML patients in Canada.

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

   Answer: 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.

   Answer: 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
None – to date we have not received any funding from Novartis since 2015.				

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: Cheryl-Anne Simoneau
Position: President
Patient Group: The Chronic Myelogenous Leukemia Society of Canada
Date: March 17, 2025

CADTH

Patient Input Template for CADTH Reimbursement Reviews

Name of Drug: asciminib (Scemblix)
Indication: For the treatment of adult patients with newly diagnosed or previously treated Philadelphia chromosome-positive CML in chronic phase.
Name of Patient Group: The Leukemia & Lymphoma Society of Canada (LLSC) and The Canadian CML Network
Author of Submission: Colleen McMillan, LLSC

1. About Your Patient Group

The Leukemia & Lymphoma Society of Canada - bloodcancers.ca
LLSC is a national charitable status organization dedicated to finding a cure for blood cancers and its ability to improve the quality of life of people affected by blood cancers and their families by funding life-enhancing research and providing educational resources, services, and support. The Leukemia and Lymphoma Society of Canada is the largest charitable organization in Canada dedicated to blood cancer, our focus includes:

- Funding research from bench to bedside.
- Rethinking how a person navigates their blood cancer experience
- Providing targeted blood cancer information
- Offering tools for psychological and emotional support
- Empowering Canadians to take charge of their blood cancer experience through practical support and advocacy

The Canadian CML Network - cmlnetwork.ca
The Canadian CML Network is a national organization focused on supporting people who live with chronic myelogenous leukemia (CML). The Canadian CML Network provides social and educational support to patients and their families, empowering them to advocate for their health and live the best life they can with CML.

2. Information Gathering

One online survey was created through SurveyMonkey. Information was gathered from February to March 2025. The survey was developed and distributed by LLSC and the Canadian CML Network, in English only. The survey was distributed through various social media channels and directly by email.

The survey asked for input from patients and caregivers who have lived experience with CML.

81 respondents participated in this survey. The majority of respondents (80/81) indicated that they were the CML patient (past or present). 1 respondent indicated that they were a caregiver of a CML patient (past or present), however this 1 respondent did not continue with the rest of the survey.

Respondents were asked to identify their age range at the time of CML diagnosis. 1 respondent answered that they were between ages 0-17 at diagnosis. This respondent was disqualified from the survey. The age demographic breakdown of respondents is shown in the chart below.

ANSWER CHOICES	RESPONSES	
0-17	1.25%	1
18-30	5.00%	4
31-44	26.25%	21
45-64	45.00%	36
65-74	18.75%	15
75+	3.75%	3
TOTAL		80

52/70 (74.29%) respondents answered that their CML was diagnosed as Philadelphia Chromosome-Positive.

49/70 (70%) answered that their CML is in the chronic phase.

70 respondents identified their primary residence: Ontario (21), British Columbia (15), Alberta (14), Quebec (9), Nova Scotia (6), Newfoundland, New Brunswick, Manitoba, Saskatchewan and Nunavut (1 in each region).

LLSC conducted two one-on-one interviews with patients currently living with CML, as well as a roundtable discussion with three additional patients who are also living with the condition. All three participants in the roundtable are currently receiving treatment with asciminib.

3. Disease Experience

A CML diagnosis is often unexpected, with patients experiencing a variety of symptoms that may seem unrelated to cancer, or sometimes no symptoms at all. The emotional impact of the diagnosis is profound, as many patients face an overwhelming sense of uncertainty and fear.

Interviewees shared their personal experiences and the moment they learned they had CML, offering a glimpse into the emotional and physical toll of the disease.

- “The first sign that something was wrong was I felt a lump below my rib cage, and it turned out that lump was my spleen, which was enlarged. The initial shock, when you hear something like that, you know, you hear leukemia and all I thought was, well, I'm going to die because that's what happens when you get leukemia because you don't know any better.”

- “Prior to the diagnosis, I was in grade 12, in 2002, getting ready to graduate high school. I was exercising a lot, trying to be fit, and I thought the weight loss was because of that. Then I started having flu-like symptoms. Then my gums were bleeding, and I had an earache. I just felt very unwell, and I ended up passing out in the shower. I went to the ER, and they did a bunch of tests. 18 to 20 hours later they said it's a form of leukemia.
I'm from Glace Bay in Cape Breton. The emergency room there is very small, so I had to go to Halifax, to the bigger hospital. Within two days I saw a hematologist and got the diagnosis of CML. At that time, they shared with me that only 2 out of 100,000 Canadians a year were diagnosed, and typically men over 50. I was a 17-year-old female, and they were kind of blown away. It was very scary because at the hospital when the doctor told us, it's a form of leukemia, my mom lost it. And at my young age was like, ‘How does that work? Why is this happening? I'm 17, I'm going to die of cancer. I'm going to lose my hair for my graduation.’ I was devastated because you just think the worst. I just remember being like ‘What does this mean and how do I fix it? What do I have to do?’
I asked my mom and dad to leave at one point because they were so upset, and I just couldn’t focus. I remember coming home from the hospital and my whole family was there. I will never forget it; it feels like yesterday. I felt like I was walking into my own funeral service. Everybody was sitting there crying, talking about me and I was like, ‘I'm still here and I don't even know what this means!’ I was out of school for 2 weeks and I remember going back to school after finding out and it was just like a weird scene from a movie where everyone was looking at me and whispering and wondering what was

happening. And I'm like, 'I've got two months left in this place and this is going to be my experience?'"

The experience of living with CML varied widely among our survey respondents. Some were more recently diagnosed, while others have been managing the disease for many years.

Respondents were asked how long they have been living with CML, and the results showed a range of experiences:

3/70 (4.29%) -- less than one year
27/70 (38.57%) – 1-5 years
18/70 (25.71%) – 6-10 years
22/70 (31.43%) -- more than 10 years

The number of treatment lines patients have undergone also varied, reflecting the ongoing challenge of managing CML and the need for alternative therapies when resistance or side effects occur. This highlights the evolving nature of CML treatment, and the continuous efforts required to find the most effective therapy for each patient.

Respondents were asked, How many lines of treatment have you for received for CML?

26/70 (37.14%) – 1 line
16/70 (22.86%) – 2 lines
11/70 (15.71%) – 3 lines
13/70 (18.57%) – 4 lines
4/70 (5.71%) – 5 lines +

Living with CML is not just about managing the disease physically; it also takes a significant emotional toll. Patients must navigate the daily challenges of managing their health while coping with the emotional burden of a chronic condition.

One interviewee reflected on the challenges of dealing with chronic fatigue, which often led to self-blame and frustration:

"I've been really hard on myself over the years. Like, why don't I want to exercise, or I don't want to eat? Just having the chronic fatigue with the chronic illness, I bring myself back, like 'you have a chronic illness! Just do what you can and get through it.'"

4. Experiences With Currently Available Treatments

The treatment for CML typically involves a range of options. This diversity in treatment reflects the individualized nature of CML management, as patients often require different approaches depending on their response to therapy and disease progression.

Respondents were asked, what types of treatment have you received for CML? Select all that apply.

58/70 (82.86%) – Tyrosine Kinase Inhibitors (TKIs)
10/70 (14.39%) – Chemotherapy
6/70 (8.57%) -- Bone Marrow/Stem Cell Transplant
11/70 (15.71%) – Answered "other" and listed treatments such as, imatinib, dasatanib, allipurinol, hydroxyurea, asciminib and radiation

TKIs are a cornerstone of CML treatment, but patients may be prescribed multiple types over the course of their treatment experience as patients may require different TKIs depending on their response to therapy and the progression of the disease.

Respondents were asked, How many TKIs have you been prescribed?

1 – 25/70 (35.71%)
2 – 11/70 (15.71%)
3 – 13/70 (18.57%)
4 or more -- 13/70 (18.57%)
I don't know – 8/70 (11.43%)

For many CML patients, finding a treatment that works without intolerable side effects can be a long and difficult journey. Some patients experience a trial-and-error process as they work with their healthcare providers to find the best therapy for their individual needs. Below, interviewees shared their experiences with various treatments and the struggles they faced with side effects and effectiveness.

- "On (my first TKI treatment) I had a lot of bone pain. It wasn't every day but when I went on a long bike ride with my family, I hardly made it back home and I could hardly walk after because the pain was so bad. That was a real reminder that I had cancer. Then (that treatment) stopped working for me about 8-12 months in, so I was switched to (another TKI). With that one, I had crazy diarrhea. I also had discoloration of my face. Certain areas of my face would tan super easy, and others wouldn't tan at all, and then unfortunately, that one stopped working after about a year or so. Then they put me on (another TKI). I was only on that one for three months because the side effects on that one were really bad. I had hair loss. I got rashes all over my body, especially on my scalp and it wasn't working either. So, then my doctor put me back on (the second TKI). It worked for about 6 months, but the side effects were even worse the second time I was on it. The diarrhea seemed more manageable the first time. The second time it was really bad. And then again, it stopped working. So, at that time, I went on asciminib and I've been on it for about a year and a half now. My hair is fine, my skin discoloration went away, and my energy levels are the best I've had."

- "I did chemo orally for four months, then I started on (the first TKI treatment) and was on (that treatment) for probably well over 10 years at 400 milligrams a day. For the side effects I had to really adjust the times throughout the day, every week because I was getting nauseous from it and I was very, very fatigued. The best time for me to take it was right after or as I ate supper. If I didn't take it with food, I would be very sick the next day or have a really bad headache. Today I'm on (a different TKI treatment). I was taking 100 milligrams and I was having a lot of side effects - chronic headaches, very, very fatigued, and I'm not prone to acne, but I was getting boils on my skin, in very odd areas, like on my head and in my private areas, things I've never seen before. And my skin was very irritable. I felt lethargic and like I was just dragging myself. If I take it before bed, I wake up with a headache and my whole body feels like heavy, so if I forget to take it earlier, I just won't take it because I know it's going to make me feel terrible the next day."

Other interviewees also elaborated on their thoughts and experiences with currently available treatments:

- "The (treatment) pill is huge! It's probably 3/4 of an inch long. They're not easy to get down. It affected all sorts of things, especially my gut. I was constantly getting diarrhea and all sorts of awful issues that went with it. I had a lot of bone pain, usually in my femurs."

- "I always had Imodium on hand, and it had to be the fast-acting Imodium for any help at all and even that would take an hour or two to work. I would just have to learn where bathrooms were because you don't know when it's going to hit, and all of a sudden, I had to be to a toilet within 5 minutes. I would wear pads lots of times just to help to protect myself. I carried underwear everywhere I went because I needed to."

Skin issues are a common side effect of some CML treatments. Many patients report a variety of skin problems, including rashes, itching, and changes in skin pigmentation.

One interviewee shared:

“On (one TKI treatment) I had a lot of itching, and I started taking a strong antihistamine. My face would feel almost burnt and I just had a rash on it, and I got these warts on my hand that had to be burnt off. I had a lot of skin issues and a lot of itching. When I started asciminib, I did have some itching but nowhere near. There is nothing noticeable on my skin and I'm not getting like, burns and stuff on my face in the same way. It’s so much better.”

Respondents were asked how CML treatment had affected their daily life and routines. The responses varied, with some patients feeling significant improvements while others faced worsened conditions due to treatment side effects:

10/40 (25%) -- Significantly improved
4/40 (10%) -- Moderately improved
10/40 (25%) -- No change
8/40 (20%) – Moderately worsened
4/40 (10%) -- Significantly worsened
4/40 (10%) – Not applicable

Some respondents elaborated on their response:

- “Due to side effects, I have been on disability”
- “Fatigue and nausea, as well as vision issues (fluid retention)”
- “Lots of tiredness, lots of infections of all kinds dry skin, dry nose, dry eyes, memory loss (short term only) White skin, Weight gain (+50lbs) Faster heartbeat while training. At first, the sun was hurting my skin, but after failing TFR and restarting (TKI treatment), it became okay! My symptoms were less important (I stopped for 4 months). I am a CEO so I would say it’s sometimes hard to mange a company and hospital visits! But it forces me to delegate more”
- “I had no symptoms of CML prior to treatment. Have had several adverse reactions to (treatment medications)”
- “I have debilitating fatigue that causes difficulty concentrating and committing to any social activities, I have bone and muscle pain, and I have increased depression and anxiety for which I am receiving treatment.”

For many patients living with CML, the impact of treatment extends beyond the physical side effects. CML treatment can also significantly affect a patient's mental health. Some reported improvements in their emotional wellbeing, while others struggle with worsened mental health due to the ongoing challenges of managing a chronic illness.

Respondents were asked, How has CML treatment affected your mental health?

6/40 (15%) -- Significantly improved
1/40 (2.5%) -- Moderately improved
19/40 (47.5%) -- No change
8/40 (20%) – Moderately worsened
3/40 (7.5%) -- Significantly worsened
3/40 (7.5%) – Not applicable

Some respondents elaborated on their response:

- “I think it gave me a form of depression. I started (an antidepressant) and I feel GREAT now! Many other symptoms that I had, I thought they were related to my TKI but in the end, I think it was depression. The hardest part of have an invisible

cancer is that your limits change a lot but people think you are healthy. My oncologist told me I would have a normal life, this is not normal at all!"

- "I don't see how these aggressive meds can heal my body. I feel vulnerable to infections and reactions have definitely affected my family and social life."

CML treatment also has a profound impact on patients' home and personal life. Many patients experience changes in their ability to engage in household activities, social interactions, and family dynamics. Below are the responses regarding how treatment has affected personal and family life:

5/40 (12.5%) -- Significantly improved
6/40 (15%) -- Moderately improved
10/40 (25%) -- No change
12/40 (30%) – Moderately worsened
2/40 (5%) -- Significantly worsened
5/40 (12.5%) – Not applicable

Some respondents elaborated on their experiences:

"I am used to a very physical life. Now I spend a lot of solitary, quiet time."

- "Fatigue Digestive issues Affect ability to do household tasks like before CML"

- "Some things improved: - My husband does more things around the house to help and he cooks every night (lucky me!) - before I was the one doing everything - My son (8 years old but 1,5 years at diagnosis) is very empathetic and enjoys taking care of his mom, but on the other hand, some bad sides: - Less libido - Tiredness so I go to bed very early and don't have much time with my husband - sometimes I can't play with my son because I am too tired and I feel guilty about it"

- "I feel vulnerable to infections and reactions. Definitely affected my family life with young grandchildren as well as social life."

- "Since I started (TKI treatment) my entire body has severe muscle spasms"

CML treatment can also impact patients' ability to maintain work both inside and outside the home. The demands of managing treatment, coupled with side effects, can make it difficult for patients to maintain regular work schedules. Below are responses regarding how CML treatment has affected respondents' ability to work both inside and outside of the home:

4/40 (10%) -- Significantly improved
4/40 (10%) -- Moderately improved
15/40 (37.5%) -- No change
10/40 (25%) – Moderately worsened
4/40 (10%) -- Significantly worsened
3/40 (7.5%) – Not applicable

Some respondents elaborated on their response:

- "I am weaker. And not strong enough to return to my job."

- “Had to reduce hours to part time and then eventually quit”
- “Difficulty concentrating as well as rapid onset of fatigue makes work impossible.”

The side effects of CML treatment can vary greatly in intensity, impacting patients’ quality of life. Respondents were asked to rate the severity of side effects they experienced during CML treatment, using a scale of “did not experience,” “mild,” “moderate,” “severe,” and “very severe.” The collective responses were measured by weighted average to determine the top five most commonly experienced and severe side effects. Below are the top 5 answers:

Fatigue – 2.69/5
Muscle, bone or joint pain – 2.07/5
Diarrhea – 2.03/5
Nausea/Vomiting – 1.75/5
Headache – 1.71/5

For some CML patients, side effects or treatment ineffectiveness may require them to stop their prescribed medications temporarily or permanently. Respondents were asked whether they had to stop taking any CML treatments for any reason.

29/40 (72.5%) – No, I have not had to stop CML treatment for any reason
2/40 (5%) – Yes, I had to stop CML treatment because I couldn't tolerate the side effects
0/40 (0%) – Yes, I had to stop CML treatment because it wasn't working for me
9/40 (22.5%) – answered “other” and some elaborated on their response:

- “I was talking (a TKI treatment) for 6 years, started having a severe reaction, but it happened just once a year. The reaction would start with very high fever, diarrhea with patches of red similar to a bad sun burn.”
- “(On one TKI): Liver problems. (Another TKI): was making me blind (papilledema)! (Current TKI treatment) works perfectly”
- “I first took (one TKI) and had to change to (another TKI) because it stopped working. I also had to interrupt (the second TKI treatment) for a period of 4 months due to severe neutropenia.”
- “Medication wasn't working, needed to go to Chemo/Radiation”
- “I stopped to try and see if I could maintain remission with treatment, sadly I had to start back on medication within 2 months”

5. Improved Outcomes

When it comes to improving outcomes for CML patients, there are several key areas that can make a significant difference. These include better long-term data on treatment effects, improved coordination of care, additional treatment options, and the importance of having a good side effect profile for treatments.

Long-Term Effects and the Need for More Data

One interviewee shared the concerns around the uncertainty of long-term effects, emphasizing the need for more data:

- “It’s that unknown of what’s going to happen later in life. We don’t have that data yet. Having more data on it would be really good.”

Coordination of Care and Patient Navigation: A significant challenge for many patients is the disconnect between different healthcare providers, which can lead to confusion about treatment options and the stress of navigating healthcare on their own.

One respondent shared their experience:

"The disconnect between doctors. I didn't know what I could do when I had travel plans. I went to my GP, and she says they're fine and I go to my hematologist who says why don't you put those plans off and that stuff is so hard. I think having someone connected to your hematologist, who's helping you navigate things rather than you having to go off on your own. And I think just the lack of acknowledgement about how anxiety producing this all is and how it impacts your general health. There's a lot on the patient to do the research to figure things out, to find solutions and it does impact your health. Just more information about resources. I didn't know with my cancer diagnosis what resources I was eligible for."

Additional Treatment Options: For patients whose current treatment options have failed, the availability of additional treatment alternatives is vital.

Interviewees expressed their relief knowing that there are other possibilities if a current treatment stops working:

"It's nice for people when medicine works then stops working because I've only ever switched medicines when they've stopped working. It hasn't been side effect based even if side effects haven't been great. It's because my BCR has started to increase on all of them. And if asciminib actually fails for me, as far as I know my next step will be meeting with the transplant team."

"It gives hope, right? And I think that's what you need. You need to have a hope that if this doesn't work, there is something else, they can do something else for you."

There is a general desire for flexibility in treatment plans, especially as individual responses to therapy can vary significantly.

Respondents were asked how important it is to have multiple treatment options available for CML:

48/58 (82.76%) -- Very important
5/58 (8.62%) – Important
1/58 (1.72%) – Somewhat important
4/58 (6.9%) – Not important

When evaluating new treatment options, several key factors are crucial for CML patients. These include maintaining a good quality of life, minimizing side effects, and ensuring treatment convenience, all of which play a vital role in effectively managing their condition.

Respondents were asked to identify the top three most important considerations, and the results were as follows:

- Quality of life during treatment: 88.15%
- Number/Severity of side effects: 74.58%
- Convenience of the treatment: 52.54%

The importance of a good side effect profile was another key consideration for respondents, further emphasizing the critical role of managing side effects in CML treatment. Respondents were asked, How important it is for a treatment to have a good side effect profile?

Very important – 44/59 (74.58%)
Important – 13/59 (22.03%)
Somewhat important – 2/59 (3.39%)

Unmet needs in CML treatment remain a critical concern for patients, and when asked to identify the most pressing challenges, respondents highlighted the following areas as the most significant gaps in current treatment options:

Fewer side effects – 35/57 (61.4%)
Improved quality of life – 30/57 (52.63%)
More tolerable treatment options – 21/57 (36.84%)

6. Experience With Drug Under Review

Among the 70 respondents, 22 (31.43%) reported having taken asciminib as a treatment for CML, with 20 continuing the survey to share detailed insights about their experiences with this treatment.

The following points outline the duration of treatment, as well as the various ways participants accessed asciminib.

Respondents were asked, How long have you been taking/did you take asciminib?

25% - 1-6 months
10% - 6-12 months
60% - 1-2 years
5% - 3+ years

Respondents were asked, how did you get access to asciminib treatment?

20% - Clinical trial
20% - Paid for by private insurance
15% - Compassionate use program (through pharmaceutical company)
45% - answered “other”. Most stated they received the treatment through their province. Others answered:

- “Out of pocket at times, and insurance through work”
- “Application to Manufacturer in Germany with supporting documentation at specific intervals.”

Respondents were asked the impact of asciminib treatment on their daily lives and routines in comparison to other treatments they have been prescribed for CML. The majority reported significant improvements, with many noting a stark contrast to the severe side effects and diminished quality of life they experienced with previous treatments. Participants shared personal accounts of how asciminib has enabled them to regain energy, reduce debilitating side effects, and improve their overall well-being.

Respondents were asked, How has asciminib treatment affected your **daily life and routines** in comparison to other treatments you have been prescribed for CML?

10/20 (50%) - Significantly improved
5/20 (25%) - Moderately improved
3/20 (15%) - No change
1/20 (5%) - Significantly worsened
1/20 (5%) - Not applicable: I have not tried other treatments for CML

Some respondents elaborated on their answer:

- "With the other treatments (TKIs), I had no quality of life. I had to stay in bed constantly; it was terrible. The symptoms included severe chronic fatigue, weakness, and dizziness. (one TKI) also caused liver problems. These three years were extremely difficult both physically and mentally. With (another TKI), I experienced a significant improvement in my energy levels, but I also had liver complications and an allergic reaction, so I had to stop. Now, with (asciminib), I am fortunate to be in molecular remission, and I’ve been able to achieve a very respectable quality of life. It changes everything! However, I’m

not sure if I will be able to return to work. I don't have much physical stamina. But overall, it's much better; there's a huge difference compared to the other treatments."

- "Since I started taking asciminib, the symptoms (side affects) have not been very severe like I experienced with the other three previous treatments."

- "I'm on a low dose of 40 mg. The side effects have been minimal compared to my experience on (a previous TKI treatment). And my BCR ABL1 results better after being on a low dose for 3 months than they were after 9 months of a full dose of (previous TKI treatment)."

- "This is the best TK I have been on by far. I feel the most like myself on this TKI than any other TK I have been on"

- "(3 previously tried TKI treatments) have unwanted side effects which made my life miserable, to the point that my physical health was threatened or the quality of life needed to hang in there, just was not there. The only negative side effect I have encountered with asciminib are muscle weakness and joint pain. They have now subsided substantially. Quality of life is definitely on the way up :). I wish I had asciminib 15 years ago when I was diagnosed."

For many patients, managing a chronic illness like CML can be emotionally challenging, with feelings of uncertainty and fear often accompanying treatment regimens. Asciminib has provided a notable shift for some, offering not only physical relief but also improved mental health, as patients reported a reduction in the anxiety, depression, and isolation that often accompany more severe side effects from other treatments.

Respondents were asked, How has asciminib treatment affected your **mental health** in comparison to other treatments you have been prescribed for CML?

6/20 (30%) - Significantly improved
4/20 (20%) - Moderately improved
7/20 (35%) - No change
2/20 (10%) - Moderately worsened
1/20 (5%) - Not applicable: I have not tried other treatments for CML

Some respondents elaborated on their answer:

- "Given that I've regained almost a normal life, it has significantly improved my mental health as well as the mental health of my immediate family. With the other treatments, I was afraid I might fall into depression because the adjustment was extremely difficult. Having to sleep 12-14 hours a day was a very tough experience. Despite all those hours of sleep, I was not functional at all. Now, with (asciminib), I only need to sleep 8 hours a night and sometimes take a one-hour nap in the afternoon, and I'm functional. I can do household chores, go for a walk, have family members over for a meal, etc."

- "I feel more confident that I will live longer and am planning travel and for now continuing to work as a nurse educator and clinical instructor at a School of Nursing in the east coast of Canada. I feel happier doing so, as there is a shortage of health care professionals, and I am helping to build the profession of nursing."

For CML patients, the impact of treatment extends far beyond just managing the disease. Effective therapies can significantly influence various aspects of daily life, including physical well-being, emotional health, and personal routines. Improvements in treatment can lead to increased mobility, better social engagement, and a greater sense of control over life's activities, ultimately contributing to an enhanced quality of life.

Respondents were asked, How has asciminib treatment affected your **home/personal life** in comparison to other treatments you have been prescribed for CML?

6/20 (30%) - Significantly improved
3/20 (15%) - Moderately improved
9/20 (45%) - No change
1/20 (5%) - Moderately worsened
1/20 (5%) - Not applicable: I have not tried other treatments for CML

Some respondents elaborated on their answer:

- “When I had side effects and complications from the previous CML treatments I was scared, afraid that there was nothing else that could help me stay healthy. I saw a social work and was fearful of my potential inability to purchase the drugs. I was sad and somewhat lonely although I kept up a "good" front. Being on Asciminib for some time now, and having good blood work results with the dosage cut in half, I am more positive, more optimistic. I am planning to drive across Canada this spring/summer. I bought a new vehicle last May and am ready to hit the road as a solo traveller. I will plan with the 3 hour driving limit each day and take my time to enjoy the experience. While on one of the other medications as treatment, the side effects and changing doses and meds prevented my from getting travel insurance (changes would reflect on me not being stable) and caused me to cancel a long awaited visit to Australia and New Zealand to see my son at Christmas time. I felt like I had no control over anything. Now, on asciminib, I am not worried the same. I went to Sweden twice to visit my son in the last two years and will do the same this year. I make 3-7 day travels to the US (or did before they brought on this tariff business), and I will go to Europe for my son's wedding in summer 2026.”

- “Having less pain, fewer side effects, less fatigue and sleeping better means I've been able to socialize more, attend public events, and contribute more to household duties. I'm physically stronger and have more endurance so I'm able to be more physically active, to travel and visit family.”

The impact of asciminib treatment on work-related activities, both inside and outside of the home, is another important consideration for patients. For many, the ability to maintain a consistent work routine or return to work is a key aspect of managing CML. Asciminib treatment has impacted some patients' ability to engage in both work-related and daily activities, highlighting the treatment's potential to support patients in maintaining their professional lives and overall sense of productivity.

Respondents were asked, How has asciminib treatment affected your ability to work, both inside and outside of the home, in comparison to other treatments you have been prescribed for CML?

5/20 (25%) - Significantly improved
3/20 (15%) - Moderately improved
11/20 (55%) - No change
1/20 (5%) - Not applicable: I have not tried other treatments for CML

In terms of side effects, respondents generally reported a mild to moderate experience with asciminib treatment. The majority of participants indicated that asciminib's side effects were either significantly better or somewhat better than side effects they experienced with previous treatments. This suggests that asciminib may offer a more manageable side effect profile for many patients, allowing them to maintain a higher quality of life compared to previous treatments.

Respondents were asked to rate the severity of side effects they experienced during asciminib treatment as; did not experience, mild, moderate, severe, very severe. Collective responses were measured by weighted average. The top 5 answers were:

Fatigue – 2.8/5

Muscle, bone or joint pain – 2.25/5
Cold symptoms (stuffy nose, sneezing, sore throat) – 1.95/5
Headache – 1.75/5
Low blood cell counts – 1.75/5

Respondents were asked, How would you compare the side effects of asciminib to those of any other treatments you have tried for CML?

13/20 (65%) - Significantly better
2/20 (10%) – Somewhat better
4/20 (20%) – About the same
1/20 (5%) – Not applicable: I have tried no other treatments for CML

Some respondents elaborated on their answer:

- "The side effects from the other treatments limited my capacity to move, socialize, or think or focus. I was constantly brain fogged and fatigued. I always preferred to be isolation and withdrawn from society and the recreational activities."
- "Some of the other side effects from other medicines has been very bad diarrhea, some joint pain, very heavy limbs. I don't experience many side effects on asciminib."
- "I have had many issues with previous treatments, pancreatitis, diarrhea, plural effusion, cardiopulmonary effusion, the list goes on"

Switching to asciminib has led to noticeable improvements for many patients, with many reporting changes that enhanced their overall well-being. The transition often resulted in a reduction of side effects, particularly those experienced with previous treatments, and several individuals noted improvements in their general health and blood work. Additionally, the ability to adjust the dosage of asciminib has provided some patients with an opportunity to further reduce side effects while maintaining positive treatment outcomes, helping them to feel better and more in control of their health.

Interviewees described various improvements they experienced after switching to asciminib from previous CML treatments:

- "After 4 months on asciminib my energy is better, and my hair is growing back."
- "When moving from (previous TKI treatment) to asciminib, it was immediate that I noticed a difference. As soon as I went off (previous TKI treatment) the diarrhea stopped, and no new side effects started. I'm happy with asciminib and I hope that other people have access to it."
- "The change was pretty immediate. Even my basic blood work got better than it had been, ever. And then my BCR tests were better than they'd ever been, and that was in a really short time. The side effects, other than a few maybe the first month or first six weeks but then really nothing that at all impacts my quality of life."
- "My BCR has been better on asciminib than any other treatments."
- One interviewee commented on the effectiveness of a dose adjustment of asciminib that helped to lessen her side effects without impacting her positive results…

- “Being able to change the dose (of asciminib) from 80mg to 40mg without it changing my blood work, I think that's a really positive thing and when we did that, I immediately felt better. Not the same day, but over a short period of time. In terms of the amount of pain I was having and fatigue, all of those things improved when I went on a lower dose and the dose is working because we've checked it”.

Respondents were asked about any interruptions in their asciminib treatment, including whether they had to stop taking the medication for any reason. The following section outlines the experiences of those who either continued or had to temporarily or permanently discontinue asciminib, as well as the reasons behind any treatment interruptions.

14/20 (70%) – No, I am still being treated with asciminib
2/20 (10%) – Yes, I had to stop asciminib treatment because it wasn't working for me
4/20 (20%) -- answered “other” and commented:

- “When I first started asciminib in April 2023, I was taking 80 mg once a day. Within a few weeks platelets drop below 50, the allowable level for the clinical trial. I was taken off it until platelets increased. In June 2023 I was prescribed 40 mg once daily. I have been on this dosage since then. In June 2024 BCR-ABL number started to improve from > 10% to 4.6% as February 2025. Slow progress but I feel good - no side effects that impede my daily life”
- “Had to stop at first because of difficulty breathing when started the first month, then tried again for a smaller dose increasing until 80 mg per day. Now I am still being treated with asciminib at 80 mg per day.”
- “At times couldn't afford it”

Respondents were asked to rate the effectiveness of asciminib in controlling their CML, as well as to evaluate its impact on their overall quality of life compared to other treatments. The responses revealed a range of experiences, highlighting both the effectiveness of the treatment and its potential to improve quality of life for many patients.

Respondents were asked, How effective was/is asciminib in controlling your CML?

2/20 (10%) – Not effective at all
4/20 (20%) – Slightly effective
3/20 (15%) – Moderately effective
3/20 (15%) – Very effective
8/20 (40%) – Extremely effective

Respondents were asked, To what extent do you agree with the following statement: "Asciminib improved my overall quality of life compared to other CML treatments”

1/20 (5%) -- Completely disagree
2/20 (10%) – Somewhat disagree
1/20 (5%) – Neutral
5/20 (25%) – Somewhat agree
11/20 (55%) – Completely agree

Respondents were asked whether they would recommend asciminib to others with CML based on their own treatment experiences. The overwhelming majority expressed strong support for the medication, citing significant improvements in their quality of life and overall health. Many shared personal stories of how asciminib positively impacted their daily routines and well-being, with some describing it as life changing.

Respondents were asked, based on your experience with asciminib treatment, would you recommend it to others with CML?

19/20 (95%) – Yes
1/20 (5%) – No

Some respondents elaborated on their answer:

- "Asciminib (Scemblix) has changed my life, nothing less. I had no quality of life with the other treatments. I was extremely sad, and everything was difficult (even the smallest household task or a visit at home). Now, I have more energy. I still feel fatigued, but I manage to have good days. For me, the happy outcome with Scemblix is equivalent to a miracle. I hope the treatment will be included in the public healthcare system. Thank you for your efforts."

- “When the other CML treatment drugs are producing side effects and the only option is Asciminib, it should be offered and available. I absolutely recommend it.”

- “I would highly recommend asciminib to anyone with CML”

- “One difficulty with the origin of symptoms in my case is my age, with the disease and the medication. What was a great surprise is the improvement of my BCR to 4.5 from 3.7.”

- “Absolutely Yes! When I was on (two previous TKI treatments), I wanted to die. (One previous TKI treatment) did a number on my cardio. Asciminib, on the other hand, is no problem.”

7. Companion Diagnostic Test

8. Anything Else?

Throughout the survey and interviews, respondents shared valuable insights into their experiences with asciminib treatment for CML, noting both physical and emotional improvements. Many reported significant benefits, including fewer side effects, increased energy, and better overall quality of life compared to previous treatments. Patients also highlighted the ability to better manage daily life, both personally and professionally. However, living with CML remains emotionally challenging, with feelings of uncertainty and the looming question of how long the treatment will remain effective.

One individual reflected on the emotional toll of this uncertainty:

"It's kind of like a roller coaster. All of the time. You know, medicines start to work, you kind of get into a decent place in life, medicines stop working, and it gets stressful. Having young kids, it's like, ‘Am I ever going to see my kids graduate from school, and get married and have kids? Will I be around for those milestones?’ My oldest son graduated last year and probably more than some people, I really cherish being at those milestones, when I get to make it to milestones because in the back of your mind, it’s always like, this may not last forever. These medicines stop working. There's only so many of them. When things go well, I think sometimes you can forget about it to a point, but as soon as they start not going well, it's like, ‘Well, how long am I going to be around? What am I going to miss?’ That’s kind of always there a little bit."

The effectiveness of asciminib has provided much-needed relief and improved well-being for many. Based on these experiences, the Leukemia & Lymphoma Society of Canada (LLSC) and the Canadian CML Network strongly urge the CDA to recommend reimbursement for asciminib treatment for adult patients with newly diagnosed or previously treated Philadelphia chromosome-positive CML in chronic phase.

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 2 years AND who may have direct or indirect interest in the drug under review.

Table 1: Financial Disclosures

Check Appropriate Dollar Range With an X. Add additional rows if necessary.

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Novartis				X
Pfizer				X
Bristol Myers Squibb				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.

Name: Colleen McMillan
Position: Advocacy Lead
Patient Group: The Leukemia & Lymphoma Society of Canada (LLSC) and The Canadian CML Network
Date: **March 24, 2025**

Canada's Drug Agency
L'Agence des médicaments du Canada
Drugs. Health Technologies and Systems. Médicaments, technologies de la santé et systèmes.

Reimbursement Review

Clinician Group Input

Project Number: PC0418-000
Generic Drug Name (Brand Name): Asciminib (Scemblix)
Indication: For the treatment of adult patients with newly diagnosed or previously treated Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP).
Name of Clinician Group: Canadian CML Physicians Interest Group
Author of Submission: Dr. Dennis Kim and Dr. Brian Leber

1. About Your Clinician Group

This submission represents a large group of physicians from academic and community centers across Canada (excluding Quebec, which has submitted independently), all with extensive experience in treating chronic myeloid leukemia (CML) and utilizing all currently available treatment options.

2. Information Gathering

Our recommendations for asciminib in CML-CP are based on virtual discussions, literature reviews, and expert analysis. We draw on clinical trial data, insights from global hematology congresses, real-world evidence (RWE) and our collective experience. Beyond scientific evaluation, these recommendations reflect our commitment to patient advocacy and better treatment access. With decades of expertise in CML-CP management, we provide a balanced, evidence-driven perspective on asciminib's role in personalized cancer care.

3. Current Treatments and Treatment Goals

TKIs are the gold standard for the treatment of CML

The introduction of tyrosine kinase inhibitors (TKIs) transformed CML from a fatal disease into a manageable chronic condition. Before TKIs were introduced, treatment options were limited, and most patients progressed from the chronic phase (CML-CP) to accelerated or blast phase within three to five years. This changed with imatinib, the first TKI targeting the BCR-ABL1 fusion protein, which revolutionized CML treatment by achieving high hematologic and cytogenetic remission rates. Following imatinib, second-generation TKIs (2G-TKIs)—dasatinib, nilotinib, and bosutinib—were developed, offering greater potency and overcoming some resistance mechanisms. BCR-ABL1 kinase domain mutation status, prior toxicities, and patient-specific factors guide treatment selection. Switching between different TKIs sometimes effectively reduces the adverse events (AEs) that lead to intolerance. However, many of these AEs are due to a class effect, as all these TKIs have a similar binding pocket on the ABL1 oncogene that cross-reacts with similar pockets on other TKIs. Furthermore, this shared binding mode also limits their ability to address certain resistance mutations. Amongst these TKIs, ponatinib is the only one effective against the T315I mutation but carries a significant risk of arterial thrombotic events.

Asciminib is a novel allosteric inhibitor targeting the myristoyl pocket of ABL1 rather than the kinase domain that is the target of all other available TKIs. Thus, this introduces a new mechanism of action for treating CML-CP patients. While the Food and Drug Administration (FDA) has approved its use in first-line (1L) therapy in the U.S, in Canada, asciminib is only indicated and funded for patients with multiple TKI failures as data for 1L therapy was not mature enough at the time of its initial review [1]. Though, special access can be granted for patients with the T315I mutation when cardiovascular risk status is a concern.

In Canada, standard 1L treatment for CML-CP includes imatinib, dasatinib, nilotinib, or bosutinib, though access varies by province (e.g., bosutinib is not available in Alberta or Ontario as frontline therapy). This differs slightly from NCCN guidelines, which recommend 2G-TKIs for patients at intermediate to high risk of progression [2]. Additional TKIs like asciminib and ponatinib are both approved for later lines of therapy, including for patients with the T315I mutation, which confers resistance to 1L options.

Physicians use BCR::ABL1 transcript levels as a surrogate marker for treatment efficacy and long-term survival in CML. This molecular response is measured using quantitative PCR (qPCR) on the International Scale (IS), with deeper reductions in BCR::ABL1 levels correlating with lower risks of progression and better survival outcomes. Patients who achieve major molecular response (MMR; BCR::ABL1 ≤0.1%) have significantly improved long-term survival, while those reaching deep molecular response (DMR; MR4 ≤0.01%, MR4.5 ≤0.0032%) have an even lower risk of relapse. Notably, a deep and sustained molecular response can make patients eligible for treatment-free remission (TFR), as patients maintaining MR4 or deeper for at least two years have the highest likelihood of successfully discontinuing therapy while remaining in remission [3].

The variety of TKIs now available for the treatment of CML-CP have allowed treatment goals to evolve from simply controlling the disease to achieving optimal therapeutic outcomes. **The main goals for therapy are to prolong survival, prevent disease progression to accelerated- or blast-phase CML, achieve response milestones (i.e. MMR and DMR), improve or maintain quality of life (QOL), minimize treatment-related toxicities, and offer eligible patients the opportunity to attempt TFR [4]For Individual patients, treatment goals evolve over time and across lines of therapy but are based on patient—and disease-specific characteristics and wishes.**>

4. Treatment Gaps (unmet needs)

4.1. Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.

Need for a better tolerated TKI

Despite the transformative impact of TKI therapy in CML, treatment failure remains a persistent issue across all lines of therapy, leading to continued CML-related mortality. It is estimated that 29,930 people worldwide died of CML in 2019 [5]. In 1L treatment, nearly **a third of patients require a switch to another TKI within the first year of treatment; a large proportion of this is due to intolerance to the initial treatment** [4,6]. Treatment switching in 1L indicates that the treatment choice at that stage was not optimal [7]. While TFR is possible, only 20% of patients achieve it. This leaves the vast majority reliant on long-term (often lifelong) TKI therapy, with its associated toxicity concerns [8]. **Even mild AEs can become intolerable over time in the context of lifelong treatment**. Intolerance is not just a challenge in 1L therapy but remains a leading cause of discontinuation across all treatment lines, as shown in American and Quebec-based data [9,10]. This underscores the urgent need for more tolerable treatment options that support long-term adherence and effective disease control for all lines of therapy.

Paradoxically, while imatinib has the most favorable cardiovascular risk profile among available TKIs and remains a common first-line choice, it has a higher discontinuation rate compared to 2G-TKIs [11,12]. This is primarily due to gastrointestinal intolerance, which is especially problematic given the chronic, year-long administration required for adequate CML control. This issue is even more pronounced for patients who switch to generic imatinib, as a retrospective study conducted in Quebec showed lower persistence rates compared to brand name imatinib [13]. **It is well recognized that high-risk patients benefit from 2G-TKIs due to their faster and deeper molecular responses, but these agents come with higher toxicity**, including cardiovascular complications (nilotinib) and pulmonary issues (dasatinib) [2,14]. This trade-off between efficacy, tolerability, and toxicity underscores the need for a better front-line option.

For many patients requiring 2L therapy, cumulative toxicity and intolerance present significant challenges. Most 1L **treatment failures result from intolerance rather than resistance, meaning switching to another ATP-binding pocket-competitive TKI often introduces new toxicities rather than solving the underlying issue.** While 2G-TKIs provide an alternative to imatinib, each has its own set of AEs—cardiovascular risks with nilotinib, pulmonary toxicities with dasatinib, and gastrointestinal issues with bosutinib. This cycle of toxicity and intolerance can lead to poor adherence, dose reductions, or discontinuation, compromising tolerability which further complicates long-term disease management and increasing the likelihood of treatment failure. A Quebec registry-based study reported that **2L therapy is commonly used but often discontinued prematurely, more frequently due to intolerance than resistance**; serial intolerance is 6.6 times more frequent than serial resistance, suggesting a class effect for intolerance in some patients [10]. There is, therefore, a significant unmet medical need for many patients for the availability of a well-tolerated option in 2L therapy.

In cases of true resistance, particularly those driven by BCR-ABL1 kinase-domain mutations like T315I, treatment options become even more restricted. This mutation confers resistance to all approved first- and 2G-TKIs except ponatinib. While ponatinib has demonstrated efficacy in this setting, its use is restricted by a high risk of arterial and venous thrombotic events, as seen in the PACE

trial [15]. Even dose-adjusted strategies in the OPTIC trial did not fully mitigate these safety concerns [16]. These limitations highlight the pressing need for a safer, highly efficacious option in 2L therapy; one that can overcome resistance without adding substantial toxicity.

Asciminib, has emerged as a promising alternative with superior efficacy, better tolerability, and a more favorable toxicity profile that has shown better tolerance compared to both imatinib and 2G-TKIs [9,11,17–19]. Notably, it also exhibits activity against T315I mutations, offering an essential option for patients with this highly resistant mutation [17,19]. However, in Canada, its approval and funding remains limited to third-line (3L) therapy, and only serves as option for patients with T315I mutations when cardiovascular risk status is an issue in prior lines of therapy. This restricts access for patients who could benefit earlier in their treatment course. Expanding asciminib's availability in earlier lines of therapy could address key unmet needs in CML management, improving patient outcomes while minimizing treatment-related burdens.

5. Place in Therapy

5.1. How would the drug under review fit into the current treatment paradigm?

Recent updates regarding asciminib studies have proven its efficacy, safety and tolerability beyond simply the 3L setting.

Asciminib is a solid contender for SOC in 1L

At the 2024 American Society of Hematology (ASH) Annual Meeting, updated results from the ASC4FIRST study confirmed asciminib's sustained superiority over investigator-selected TKIs (IS-TKIs) (imatinib or 2G-TKIs) in 1L treatment of CML-CP [11]. The trial was unique as the IS-TKI design allowed physicians to choose the comparator TKI based on individual patient factors. This approach better reflects real-world clinical decision-making compared to traditional fixed-comparator trials. Instead of limiting the control arm to a single TKI, ASC4FIRST allowed investigators to select imatinib or a 2G-TKI (bosutinib, dasatinib, or nilotinib) as the comparator, ensuring that patients received a TKI suited to their risk profile and comorbidities.

Consistent with prior reported results, in this 96-week update, MMR rates, a critical milestone associated with long-term disease control and reduced risk of progression, remained significantly higher with asciminib (74.1%) compared to IS-TKIs (52.0%), with a 22.4% difference (P < .001). This improvement was seen across the imatinib (76.2% vs. 47.1% [95% CI, 17.6-41.8 P< .001]) and 2G-TKI (72.0% vs. 56.9% [95% CI, 2.3-28.0]) strata. Although not statistically significant regarding 2G-TKIs, the gap in response with this control arm appeared to widen with time (figure 1). Investigators also noted that asciminib outperformed IS-TKIs across all patient subgroups, reinforcing its broad efficacy regardless of risk score, demographics, or cardiovascular risk. It is important to note that asciminib also induced faster and deeper molecular response than IS-TKIs, with 48.8% of asciminib-treated patients achieving MR4 and 30.9% reached MR4.5, compared to 27.5% and 17.7% in the IS-TKI group. These faster deep responses raise the possibility of having more patients attempting TFR in the future.

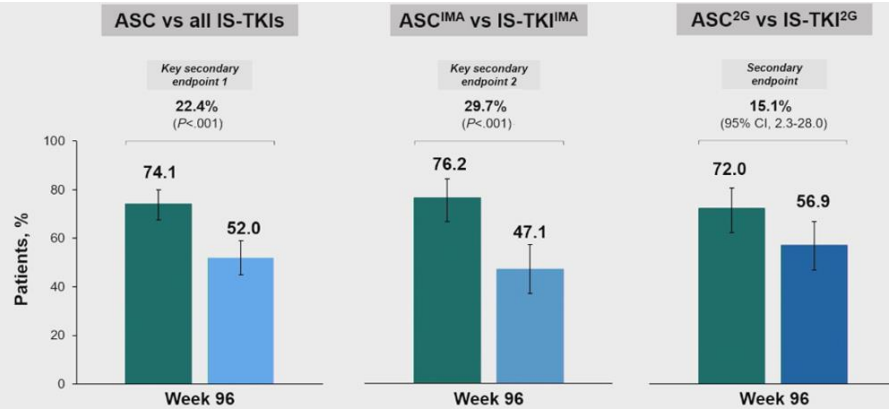

Figure 1. MMR rate at week 48 and 96 of asciminib in 1L vs all IS-TKIs or vs imatinib or 2G-TKIs. Results are taken from [11]. 2G, 2G-TKI; ASC, asciminib; IMA, imatinib; IS-TKI, investigator-selected TKI.

By the 96-week data cutoff, **treatment discontinuation due to AEs was 54% lower with asciminib compared to IS-TKIs** (table I), a trend observed in both the imatinib and 2G-TKI groups. In terms of severe AEs (grade 3 or higher), asciminib had fewer cases

(44.5%) than both imatinib (49.5%) and 2G-TKIs (59.8%). Arterial occlusive events were rare, with only a few cases in the asciminib and 2G-TKI groups. These results suggest that, **for the first time, a more potent TKI demonstrates superior efficacy without sacrificing tolerability and safety compared to all available TKIs in 1L**. With its favorable risk-benefit profile, asciminib is a strong candidate for 1L treatment in newly diagnosed CML-CP and a potential new standard of care.

Table I. Treatment discontinuation with asciminib in 1L vs all IS-TKIs or vs imatinib or 2G-TKIs. Results are taken from [11]. 2G, 2G-TKI; ASC, asciminib; IMA, imatinib; IS-TKI, investigator-selected TKI; ELN, electronic laboratory notebook.

Randomized patients, %	Asciminib			IS-TKIs		
	ASC (n=201)	ASC^{IMA} (n=101)	ASC^{2G} (n=100)	All IS-TKIs (n=204)	IS-TKI^{IMA} (n=102)	IS-TKI^{2G} (n=102)
Treatment ongoing	81.6	82.2	81.0	60.3	52.0	68.6
Discontinued from treatment	17.9	16.8	19.0	38.2	46.1	30.4
Unsatisfactory therapeutic effect	9.5	7.9	11.0	20.6	28.4	12.7
Treatment failure per ELN	5.0	5.9	4.0	13.7	18.6	8.8
Confirmed loss of MMR	2.0	2.0	2.0	1.5	2.0	1.0
Other	2.5	0	5.0	5.4	7.8	2.9
Adverse event	6.0	5.9	6.0	12.7	12.7	12.7
Progressive disease	1.0	2.0	0	2.0	2.9	1.0
Physician decision	0.5	0	1.0	0	0	0
Protocol deviation	0.5	1.0	0	1.0	1.0	1.0
Patient decision	0.5	0	1.0	1.5	1.0	2.0
Pregnancy	0	0	0	0.5	0	1.0

Asciminib for 2L CML-CP treatment

The ASC2ESCALATE study is the first prospective trial of asciminib in 2L treatment for CML. In this ongoing trial, 71 patients who switched from a prior TKI due to resistance (55%) or intolerance (45%) started asciminib at 80 mg once daily, with potential dose escalation based on individual responses [18]. The interim results presented at ASH 2024 showed that a**t a relatively short follow-up duration of 4.5 months, 95% remained on treatment**, with only two requiring dose escalation. This high retention rate is notable as most treatment discontinuations with asciminib due to drug AEs occur usually within the first six months [19]. By six months, 43% achieved MMR, consistent with earlier studies (figure 2). The safety profile was favorable, with Grade ≥3 adverse events in 16.3% of patients, most commonly hypertension (11%). Only one patient discontinued due to Grade 3 vomiting, and thrombocytopenia (5%) occurred less frequently than in previous trials. This is in steep contrast with other TKIs where a Quebec study showed that nearly 50% of patients discontinue their treatment [10]. Notably, no arterial occlusive events or deaths were reported.

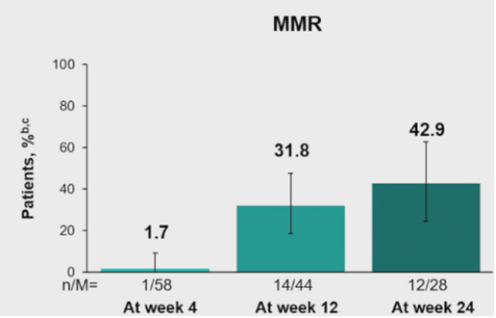

Figure 2. MMR rate at week 4, 12 and 24 weeks of asciminib in 2L. Results are taken from [18].

While data from ASC2ESCALATE is still maturing, RWE from the U.S. supports its findings with a longer follow-up. In a retrospective study of 149 patients receiving asciminib in 2L, 93.3% remained on treatment at 48 weeks, confirming its tolerability. Molecular response rates were high, with 87.8% achieving MR2 and 68.2% reaching MMR or better. The safety profile mirrored ASC2ESCALATE, showing a low cytopenia rate (4%) and no progression to accelerated or blast phase of the disease. These findings

further establish asciminib as a well-tolerated and effective 2L treatment for CML, reinforcing the promising early data from ASC2ESCALATE. Regardless of whether patients switched due to resistance or intolerance, asciminib consistently demonstrated rapid and durable responses, aligning with the phase 3 ASC4FIRST trial and confirming its efficacy across multiple lines of therapy.

As clinicians with decades of experience treating CML, we have had the opportunity to prescribe asciminib in the 2L setting through alternative funding mechanisms such as self-pay, private insurance, and compassionate access. **Our collective experience in Canada strongly aligns with the favorable results observed in clinical trials**, further demonstrating that asciminib is an effective and well-tolerated treatment option for patients who experience resistance or intolerance to 1L therapy. **The fact that some clinicians have sought access to asciminib through private insurance or other channels underscores the urgent need for its availability in the 2L setting, particularly for patients who are contraindicated for other TKI therapies due to comorbidities or other factors.**

Therefore, based on the positive efficacy, safety and tolerance outcomes of the ASC4FIRST, ASC2ESCALTAE, U.S.-RWE trials and our own experience, we recommend that asciminib is to be made available as a 1L and 2L treatment option for patients with CML-CP.

5.2. Which patients would be best suited for treatment with the drug under review? Which patients would be least suitable for treatment with the drug under review?

We recommend asciminib be made available for all CML-CP patients that fit the criteria for ASC4FIRST in 1L and ASC2ESCALATE in 2L and this regardless of whether progression was caused by resistance, intolerance or lack of response.

Least suitable patient populations would include those contraindicated in the product monograph.

5.3 What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?

Monitoring for lack of response would occur when clinically indicated, as per the current standard of care. Currently, most Canadian physicians follow the European LeukemiaNet recommendations to guide decision-making [14]. Response assessment begins before treatment initiation with baseline qPCR and mutation testing if resistance is suspected. During the first 12 months, qPCR should be performed every three months and a change in treatment is recommended when intolerance cannot be ameliorated or when molecular milestones are not reached. Beyond 12 months, BCR::ABL1 levels should be monitored every three to six months to ensure continued response. If a loss of response occurs, monitoring should be increased to every three months, and mutation testing should be performed to assess for resistance mechanisms.

5.4 What factors should be considered when deciding to discontinue treatment with the drug under review?

Therapy should be discontinued at the first sign of response failure or in the case of persistent toxicity despite dose modification per the product monograph, or intolerance. Greater than 10% BCR-ABL1 at three and six months OR greater than 1% BCR-ABL1 at 12 months or beyond indicates treatment failure [14].

5.5 What settings are appropriate for treatment with [drug under review]? Is a specialist required to diagnose, treat, and monitor patients who might receive [drug under review]?

Hematologists with experience in treating CML patients are required for the initial treatment recommendation and early monitoring of asciminib therapy. Pharmacy/nursing expertise can support the management of oral agents and routine AE screening, including assessing for treatment adherence.

6. Additional Information

No additional information. References listed below were used to support this input letter.

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7. Conflict of Interest Declarations

To maintain the objectivity and credibility of the CDA-AMC drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the clinician group input. CDA-AMC may contact your group with further questions, as needed. Please see the *Procedures for Drug Reimbursement Reviews* (section 6.3) for further details.

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

   No

2. Did you receive help from outside your clinician group to collect or analyze any information 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. **Please note that this is required for <u>each clinician</u> who contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.**

Declaration for Clinician 1

Name: Dennis Kim, MD, PhD
Position: Head of Malignant Hematology Program
Professor of Medicine, University of Toronto
Clinician Investigator, Leukemia and Allogeneic BMT Programs
Princess Margaret Cancer Centre/University Health Network
Toronto, ON

Date: March 11, 2025

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

Table 1: Conflict of Interest Declaration for Clinician 1

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Novartis Canada			X	
Sanofi Canada			X	
Pfizer	X			
Paladin	X			
Daichi-Sankyo	X			
Abbvie	X			
Jazz	X			
Astellas	X			
Ascentage	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 2

Name: Brian Leber
Position: Professor of Medicine (Hematology), McMaster University; Hematologist, Juravinskl Hospital/Cancer Centre of Hamilton Health Sciences;
Date: March 11, 2025

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

Table 3: Conflict of Interest Declaration for Clinician 2

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Pfizer		x		
Abbvie		x		
Novartis		x		
BMS/Celgene		x		
Servier		x		
AMGEN		x		
Jazz		x		
Astellas		x		
Astex	x			
Paladin	x			
Alexion/GSK		x		
Roche	x			
SOBI		x		
Janssen	x			
Otsuka	x			
Treadwell	x			
Takeda	x			
Taiho	x			

Declaration for Clinician 3

Name: Alym Abdulla
Position: Hematologist, Royal Columbian Hospital
Date: March 13, 2025

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

Table 1: Conflict of Interest Declaration for Clinician 3

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Pfizer		X		
Abbvie	X			
Sobi	X			
Medison	X			
Novartis	X			
GSK	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 4

Name: Sonia Cerquozzi
Position: Clinical Assistant Professor, University of Calgary
Date: March 19 2025

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

Table 1: Conflict of Interest Declaration for Clinician 4

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
GSK		X		
Novartis			X	
BMS	X			
Pfizer	X			
Medison Pharma Canada Inc		X		
Incyte	X			
Abbvie	X			
Celgene	X			
Jazz	X			
Takeda	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 5

Name: Thomas Dunne
Position: Hematologist, Newfoundland & Labrador Health Services; Assistant Clinical Professor, Memorial University of Newfoundland Faculty of Medicine
Date: March 18, 2025

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

Table 1: Conflict of Interest Declaration for Clinician 5

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Abbvie		x		
FORUS	x			
BMS/Celgene	x			
Apobiologix	x			
Jazz	x			
Astellas	x			
Beigene	x			
Novartis	x			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 6

Name: Dr Mohamed Elemary
Position: Hematologist, Program Director of Saskatchewan Stem Cell Transplant and Cellular Therapy
Date: March 13, 2025

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

Table 1: Conflict of Interest Declaration for Clinician 6

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Abbvie (Advisory Boards)	X			
Jazz (Advisory Boards)	X			
Novartis (Advisory Boards)	X			
BMS (Advisory Boards)	X			
Astellas (Advisory Boards)	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 7

Name: James T. England

Position: Physician Malignant Hematology Odette Cancer Centre/Assistant Professor University of Toronto

Date: 20 March 2025

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

Table 1: Conflict of Interest Declaration for Clinician 7

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
GSK	X			
Novartis	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 8

Name: Blair Ernst
Position: Hemato Oncologist, Trillium Health Partners
Date: March 17, 2025

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

Table 1: Conflict of Interest Declaration for Clinician 8

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Novartis		X		

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 9

Name: Lynda Foltz
Position: Hematologist
Date: Mar 21, 2025

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

Table 1: Conflict of Interest Declaration for Clinician 9

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Novartis		x		

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 10

Name: Dr Donna Forrest
Position: Hematologist, Leukemia/BMT Program of BC
Date: March 19, 2025

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

Table 1: Conflict of Interest Declaration for Clinician 10

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Novartis	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 11

Name: Christina Garcia da Silva Fraga

Position: Hematologist

Date: March 18, 2025

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

Table 1: Conflict of Interest Declaration for Clinician 11

Company	Check appropriate dollar range*			
	$0 to $5,000	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Novartis (speaker's grant and advisory boards		x		
GSK (advisory board)		x		
Abbvie (advisory board)	x			
Gilead-Kite (advisory board)	x			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 12

Name: Jill Fulcher
Position: Clinical Hematologist/Associate Professor
Date: 18 March 2025

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

Table 1: Conflict of Interest Declaration for Clinician 12

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Novartis	x			
Amgen		x		
AbbVie	x			
Jazz Pharmaceuticals	x			
Gilead	x			
Pfizer	x			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 13

Name: Karine Gauthier
Position: Hematologist
Date: 19 March 2025

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

Table 1: Conflict of Interest Declaration for Clinician 13

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Jazz Pharmaceuticals	X			
Sobi	X			
Novartis	X			
GlaxoSmithKline	X			
Kite/Gilead	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 14

Name: Michelle Geddes
Position: Hematologist, Clinical Associate Professor University of Calgary
Date: March 20, 2025

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

Table 1: Conflict of Interest Declaration for Clinician 14

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Novartis	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 15

Name: Kuljit Grewal
Position: Hematologist Eastern Health
Date: March 18, 2025

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

Table 1: Conflict of Interest Declaration for Clinician 15

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Novartis	X			
Alexion		X		
Sobi	X			
Amgen	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 16

Name: Dr Brian Harnett
Position: Hematologist, NL Health Services. Clinical Assistant Professor of Medicine, Memorial University of Newfoundland and Labrador
Date: March 13, 2025

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

Table 1: Conflict of Interest Declaration for Clinician 16

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Novartis	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 17

Name: Chris Hillis
Position: Hematologist
Date: March 14, 2025

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

Table 1: Conflict of Interest Declaration for Clinician 17

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
AstraZeneca		X		
Pfizer		X		
Janssen		x		
Paladin	X			
Bristol-Meyers Squibb	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 18

Name: Mark Hnatiuk
Position: Hematologist, Assistant Clinical Professor University of Alberta
Date: March 19, 2025

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

Table 1: Conflict of Interest Declaration for Clinician 18

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Novartis			X	
Pfizer			X	
GSK	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 19

Name: Kareem Jamani
Position: Clinical Assistant Professor, Attending Physician, Arthur Child Cancer Centre/University of Calgary
Date: March 16, 2025

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

Table 1: Conflict of Interest Declaration for Clinician 19

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Novartis	x			
Jazz	x			
Pfizer	x			
Takeda	x			
Sanofi	x			
Vertex	x			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 20

Name: Matthew Kang
Position: Hematologist
Date: March 17, 2025

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

Table 1: Conflict of Interest Declaration for Clinician 20

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
There is no conflict of interest				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 21

Name: Ilana Kopolovic
Position: Hematologist, Lakeridge Health Oshawa**,** Adjunct professor, University of Toronto**,** Adjunct Professor, Queens University
Date: March 18, 2025

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

Table 1: Conflict of Interest Declaration for Clinician 21

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Novartis	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 22

Name: Rouslan Kotchetkov
Position: Hematologist-Oncologist, Hudson Regional Cancer Program
Date: March 13, 2025

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

Table 1: Conflict of Interest Declaration for Clinician 22

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
There is no conflict of interest				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 23

Name: Philip Kuruvilla
Position:
Date: March 17, 2025

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

Table 1: Conflict of Interest Declaration for Clinician 23

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Novartis		x		
Pfizer	x			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 24

Name: Charles Li
Position: Consultant hematologist
Date: March 17, 2025

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

Table 1: Conflict of Interest Declaration for Clinician 24

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
NONE				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 25

Name: Kristjan Paulson
Position: Hematologist, Cancer Care Manitoba
Date: March 20, 2025

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

Table 1: Conflict of Interest Declaration for Clinician 25

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Amgen	X			
Astellas	X			
AbbVie	X			
Novartis	X			
Pfizer	X			
Sanofi	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 26

Name: Dr. Muhammad Saleem Raza
Position: Medical oncologist Dr Everett Chalmers Hospital Fredericton NB
Date: March 14, 2025

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

Table 1: Conflict of Interest Declaration for Clinician 26

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Novartis	x			
Pfyzer	X			
Jenssen	X			
BMS	X			
Forus therapeutics	X			
Apobiologix	x			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 27

Name: K. Sue Robinson
Position: Hematologist
Date: March 17,2025

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

Table 1: Conflict of Interest Declaration for Clinician 27

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Novartis	x			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 28

Name: Waleed Sabry
Position: Hematologist, Saskatoon Cancer Center. Professor Hemato-Oncology, University of Saskatchewan
Date: March 14th, 2025

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

Table 1: Conflict of Interest Declaration for Clinician 28

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Incyte	X			
GSK	X			
Novartis	X			
Janssen	X			
JAZZ		X		
Beigene		X		

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 29

Name: Lynn Savoie
Position: Associate Clinical Professor of Hematology, University of Calgary and the Arthur JE Child Comprehensive Cancer Centre
Date: March 17. 2025

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

Table 1: Conflict of Interest Declaration for Clinician 29

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Novartis			X	
BMS	X			
Jazz/Takeda	X			
Amgen	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 30

Name: Ismail Sharif
Position: Hematologist
Date: March 17, 2025

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

Table 1: Conflict of Interest Declaration for Clinician 30

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
AbbVie	X			
Novartis	X			
JAJ	X			
Amgen	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 31

Name: Shireen Sirhan
Position: MD
Date: March 19, 2025

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

Table 1: Conflict of Interest Declaration for Clinician 31

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Novartis	x			
GSK	x			
Forus Health	x			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 32

Name: Craig Speziali MD MSc FRCPC
Position: Hematologist, CancerCare Manitoba; Assistant Professor, Max Rady College of Medicine, University of Manitoba
Date: March 17, 2025

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

Table 1: Conflict of Interest Declaration for Clinician 32

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Novartis	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 33

Name: Ryan Stubbins
Position: Hematologist, Leukemia/BMT Program of BC
Date: March 17th, 2025

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

Table 1: Conflict of Interest Declaration for Clinician 33

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
AbbVie		X		
Astellas	X			
BMS	X			
Jazz Pharmaceuticals	X			
Kite/Gilead		X		
Pfizer	X			
Novartis	X			
Sobi	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 34

Name: Anargyros Xenocostas
Position: Honorary Consultant in Hematology, LRCP
Director of the Hemopoietic Stem Cell Transplant Program LHSC Associate Professor of Medicine and Oncology, Division of Hematology, LHSC-VH
Schulich School of Dentistry and Medicine, University of Western Ontario London Health Sciences-VH,
800 Commissioners Rd., E., Rm E6-215 London, Ontario N6A 4G5

Date: March 17, 2025

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

Table 1: Conflict of Interest Declaration for Clinician 34

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Novartis (Consulting over the past 12-month period)		X		

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 35

Name: Dr Sean Young, PhD DABMGG FACMG FCCMG
Position: Clinical Molecular Geneticist, Cancer Genetics Laboratory, BC Cancer
Date: 19 Mar 2025

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

Table 1: Conflict of Interest Declaration for Clinician 35

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Novartis	X			
Astellas	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 36

Name: Dr. Mohammad S. Al-Katari
Position: Complex Hematology Satff Physician at Thunder Bay Regional Cancer Care & Assistant Professor of Medicine at NOSM
Date: March 20, 2025

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

Table 1: Conflict of Interest Declaration for Clinician 36

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Novartis Pharmaceuticals Canada Inc.	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 37

Name: Stephanie Lee
Position: hematologist/assistant professor
Date: Mar 22/25

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

Table 1: Conflict of Interest Declaration for Clinician 1

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Medison		x		
Novartis	x			
Forus Therapeutics	x			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 38

Name: Dr. Nicole Laferriere
Position: Staff Hematologist, Medical Director Oncology Thunder Bay Regional Health Sciences Centre, Professor, Northern Ontario School of Medicine

Date: 21-03-2025

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

Table 1: Conflict of Interest Declaration for Clinician 1

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Astra Zeneca	X			
Alexion	X			
Amgen	X			
Astellas	X			
Abbvie	X			
Baxter	X			
Beigene	X			
Bristol Myers Squibb	X			
Celgene	X			
Forus	X			
Incyte	X			
Janssen	X			
Jazz	X			
Novartis	X			
Pfizer	X			
Roche	X			
Takeda	X			

* Place an X in the appropriate dollar range cells for each company.

CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: PC0405-000
Generic Drug Name (Brand Name): Asciminib (Scemblix)
Indication:
Manufacturer Requested Reimbursement Criteria[1]:
For adult patients with **newly diagnosed** Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP).
Name of Clinician Group: Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee
Author of Submission: Dr. Tom Kouroukis and members of the OH (CCO) Hem DAC

1. About Your Clinician Group

OH-CCO's Drug Advisory Committees provide timely evidence-based clinical and health system guidance on drug-related issues in support of CCO's mandate, including the Provincial Drug Reimbursement Programs (PDRP) and the Systemic Treatment Program.

2. Information Gathering

Information was gathered via teleconference meeting.

3. Current Treatments and Treatment Goals

Currently available 1L treatment options include other tyrosine kinase inhibitor (TKI) options.

Treatment goals – complete molecular response according to established CML guidelines, improvement in blood counts, reduction in splenomegaly and other symptoms.

4. Treatment Gaps (unmet needs)

4.1. Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.

Not all patients respond favorably to first-line TKIs. Some patients may not tolerate existing TKIs.

5. Place in Therapy

5.1. How would the drug under review fit into the current treatment paradigm?

Asciminib could be an option for first-line therapy and could become the standard of care.

5.2. Which patients would be best suited for treatment with the drug under review? Which patients would be least suitable for treatment with the drug under review?

This would be applicable to all first-line treatment for patients with CML.

5.3 What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?

Established CML response criteria and reduction in symptoms (e.g., splenomegaly).

5.4 What factors should be considered when deciding to discontinue treatment with the drug under review?

Lack of response, failure to meet establish CML response criteria, overt progression, or significant toxicities.

5.5 What settings are appropriate for treatment with [drug under review]? Is a specialist required to diagnose, treat, and monitor patients who might receive [drug under review]?

Outpatient.

Hematologists with experience in managing CML.

6. Additional Information

N/A

7. Conflict of Interest Declarations

To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the clinician group input. CADTH may contact your group with further questions, as needed. Please see the *Procedures for CADTH Drug Reimbursement Reviews* (section 6.3) for further details.

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

   OH-CCO PDRP provided secretariat function to the group.

2. Did you receive help from outside your clinician group to collect or analyze any information 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. **Please note that this is required for each clinician who contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.**

Declaration for Clinician 1

Name: Dr. Tom Kouroukis
Position: Lead, Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee
Date: 27-02-2025

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

Table 1: Conflict of Interest Declaration for Clinician 1

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Add company name				
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 2

Name: Dr. Christopher Cipkar
Position: Member, OH-CCO Hem DAC
Date: 27-02-2025

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

Table 2: Conflict of Interest Declaration for Clinician 2

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Add company name				
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 3

Name: Rami El-Sharkaway
Position: Member, OH-CCO Hem DAC
Date: 27-02-2025

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

Table 3: Conflict of Interest Declaration for Clinician 3

Company	Check appropriate dollar range*			
	$0 to $5,000	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
The Leukemia & Lymphoma Society of Canada (sponsored talk)				
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 4

Name: Dr. Jordan Herst
Position: Member, OH-CCO Hem DAC
Date: 27-02-2025

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

Table 4: Conflict of Interest Declaration for Clinician 4

Company	Check appropriate dollar range*			
	$0 to $5,000	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Add company name				
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 5

Name: Dr. Selay Lam
Position: Member, OH-CCO Hem DAC
Date: 27-02-2025

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

Table 5: Conflict of Interest Declaration for Clinician 5

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Add company name				
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 6

Name: Dr. Lee Mozessohn
Position: Member, OH-CCO Hem DAC
Date: 27-02-2025

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

Table 5: Conflict of Interest Declaration for Clinician 6

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Add company name				
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 7

Name: Dr. Guillaume Richard-Carpentier
Position: Member, OH-CCO Hem DAC
Date: 27-02-2025

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

Table 5: Conflict of Interest Declaration for Clinician 7

Company	Check appropriate dollar range*			
	$0 to $5,000	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Add company name				
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: PC0418
Generic Drug Name (Brand Name): Asciminib (Scemblix)
Indication:
Manufacturer Requested Reimbursement Criteria[1]:
For adult patients with **previously treated** Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP).
Name of Clinician Group: Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee
Author of Submission: Dr. Tom Kouroukis and members of the OH (CCO) Hem DAC

1. About Your Clinician Group

OH-CCO's Drug Advisory Committees provide timely evidence-based clinical and health system guidance on drug-related issues in support of CCO's mandate, including the Provincial Drug Reimbursement Programs (PDRP) and the Systemic Treatment Program.

2. Information Gathering

Information was gathered via teleconference meeting

3. Current Treatments and Treatment Goals

Currently available 2L treatment options include dasatinib, bosutinib, nilotinib, and if there is T315i mutation, then ponatinib.

Treatment goals – complete molecular response according to established CML guidelines, improvement in blood counts, reduction in splenomegaly and other symptoms.

4. Treatment Gaps (unmet needs)

4.1. Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.

Not all patients respond favorably to second line TKIs. Some patients may not tolerate existing TKIs.

5. Place in Therapy

5.1. How would the drug under review fit into the current treatment paradigm?

Asciminib could be an option for second line therapy.

5.2. Which patients would be best suited for treatment with the drug under review? Which patients would be least suitable for treatment with the drug under review?

This would be applicable to all second line treatment for patients with CML.

5.3 What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?

Established CML response criteria and reduction in symptoms (e.g., splenomegaly).

5.4 What factors should be considered when deciding to discontinue treatment with the drug under review?

Lack of response, failure to meet establish CML response criteria, overt progression, or significant toxicities.

5.5 What settings are appropriate for treatment with [drug under review]? Is a specialist required to diagnose, treat, and monitor patients who might receive [drug under review]?

Outpatient.

Hematologists with experience in managing CML.

6. Additional Information

N/A

7. Conflict of Interest Declarations

To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the clinician group input. CADTH may contact your group with further questions, as needed. Please see the *Procedures for CADTH Drug Reimbursement Reviews* (section 6.3) for further details.

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

   OH-CCO PDRP provided secretariat function to the group.

2. Did you receive help from outside your clinician group to collect or analyze any information 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. **Please note that this is required for each clinician who contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.**

Declaration for Clinician 1

Name: Dr. Tom Kouroukis
Position: Lead, Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee
Date: 27-02-2025

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

Table 1: Conflict of Interest Declaration for Clinician 1

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Add company name				
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 2

Name: <Enter full name>
Position: <Enter currently held position>
Date: <DD-MM-YYYY>

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

Table 2: Conflict of Interest Declaration for Clinician 2

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Add company name				
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 3

Name: <Enter full name>

Position: <Enter currently held position>
Date: <DD-MM-YYYY>

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

Table 3: Conflict of Interest Declaration for Clinician 3

Company	Check appropriate dollar range*			
	$0 to $5,000	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Add company name				
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 4

Name: <Enter full name>
Position: <Enter currently held position>
Date: <DD-MM-YYYY>

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

Table 4: Conflict of Interest Declaration for Clinician 4

Company	Check appropriate dollar range*			
	$0 to $5,000	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Add company name				
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 5

Name: <Enter full name>
Position: <Enter currently held position>
Date: <DD-MM-YYYY>

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

Table 5: Conflict of Interest Declaration for Clinician 5

Company	Check appropriate dollar range*			
	$0 to $5,000	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Add company name				
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.