CADTH REIMBURSEMENT REVIEW

Patient and Clinician Group Input

momelotinib (TBC)

(GlaxoSmithKline Inc.)

Indication: Momelotinib is indicated for the treatment of disease-related splenomegaly or symptoms, and anemia in adult patients with primary myelofibrosis, post polycythemia vera myelofibrosis or post essential thrombocythemia myelofibrosis who are Janus Kinase (JAK) inhibitor naïve or have been treated with a JAK inhibitor.

June 28, 2024

This document compiles the input submitted by patient groups and clinician groups for the file under review. The information is used by CADTH 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.

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Patient Group Input

CADTH

Patient Input Template for CADTH Reimbursement Reviews

Name of Drug: Momelotinib
Indication: Primary Myelofibrosis, Post-PV myelofibrosis, Post-ET myelofibrosis
Name of Patient Group: Heal Canada
Author of Submission: Brigitte Leonard, Ph.D and Cheryl Petruk

1. 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-centred 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/

2. Information Gathering

- **Co-author: Cheryl Petruk**
  - a former caregiver of a post-ET myelofibrosis patient
  - The MPN Canadian Network's founder, where she witnessed patients' experiences for more than 15 years.
  - Personal involvement in the international MPN landmark survey conducted in 2016, in which she secured the enrollment of 64 patients. This survey was published in 2017 with Dr Claire Harrison as the primary author.[1]
- **Interview** with Canadian myelofibrosis treaters (n=10).
- **Online survey**: Impact of frequent transfusion on Canadian patients QoL- 2024 (n=24)
- **Literature review**

PS

1) Most of the observations mentioned in this report are specific to myelofibrosis patients. However, it will be specified if the observations include all MPN types (MF, PV, ET) or another myeloid cancer.
2) In this report, we won't address differences between primary myelofibrosis, post-PV or post-ET myelofibrosis because:

- It will simplify the discussion
- Sub-types seem to have a minimal impact on risk stratification and overall survival.
- Sub-types seem have no apparent impact on response to JAKi.
- JAKi are approved for all sub-types of myelofibrosis

3. Disease Experience

Myelofibrosis, a misunderstood cancer

Often, myelofibrosis is described as a bone marrow (BM) disorder characterized by excessive scar tissue formation in the BM, splenomegaly, and constitutional symptoms. However, the understanding of myelofibrosis has evolved dramatically over the last two decades after the discovery of the critical driver mutations: JAK2 (2005), MPL (2008), and CALR (2013)

Myelofibrosis can still be perceived as an indolent disorder by physicians, and patients are undertreated. In 2017, more than five years after the approval of ruxolitinib, 51% of the physicians chose watchful waiting to manage more than 25% of their patients, including patients with high symptom burden. [1] Patients with MF have reduced survival, with a median survival of less than 6 years.[2] High- and intermediate-2–risk patients have a median life expectancy ranging from approximately 1.5 to 4 years.[3,4]

Myelofibrosis is a myeloproliferative neoplasm, a rare cancer where blood cell production is impacted by the dysregulation of the JAK-mediated signalling pathway, leading to abnormal myeloproliferation and overproduction of cytokines.[5] This stem cell cancer involves the aberrant signalling of multipotent stem cells that lead to clonal expansion, increasing the number of abnormal MEG and myeloid progenitor cells. Abnormal production of cytokines, growth factors and other signalling molecules stimulate the transformation of mesenchymal stem cells into fibroblasts. Inflammatory cytokines, such as TGF-β (transforming growth factor-beta), stimulate fibroblasts to produce extracellular matrix and collagen deposition, contributing to the fibrosis observed in myelofibrosis.[6,7] So, BM fibrosis, splenomegaly, progressively worsening anemia, and symptoms are surrogate markers and the direct consequence of the cancer progression.

Impact of myelofibrosis on patients, their family and society

Myelofibrosis is a cancer associated with a high disease burden, reduced QoL and shortened survival.
This section refers to the international landmark survey conducted in 2016 and published in 2017.[1] A total of 174 patients diagnosed with myelofibrosis have been evaluated. The Canadian MPN network, under the supervision of Cheryl Petruk, supported the recruitment of 64 patients, including 28 myelofibrosis patients.

Recruitment:
Patients have been enrolled by two methods:

- Through Patient Organizations (PO) such as the Canadian MPN network
- HCPs recommendation
    - Patients from PO reported a higher symptom burden than those recruited from HCPs
    - Patients from PO were more frequently women and younger. The authors suggested that patients recruited from PO are probably better educated about the disease.

Demographics

- The median disease duration time was four years.
- 78% of patients had been diagnosed within 2 years of experiencing symptoms.
- Risk stratification"
    - 42% of patients recruited in this survey fit the patient population studied in JAKi clinical trials (Int/High)
    - 43% of patients did know their disease-specific scores
- Patients involved in the survey could receive a treatment
    - 54% received ruxolitinib
    - 40% aspirin
    - 28% Hydroxyurea

Symptoms frequency and severity

- 83% of respondents said that MPN symptoms impacted their QoL (Table 2)
- 86% of patients would most likely have fatigue and tiredness resolved, and 58% mentioned bone pain (a symptom associated with disease progression)

Table 2- Symptoms experienced in the last 12 months[1]:

Symptom	Frequency	Severity
Fatigue	54%	6.68

Inactivity		6.7
Abdominal discomfort	30%	
Shortness of breath	29%	5.67
Night sweats	29%	
Difficulty sleeping	27%	5.53
Bruising	26%	
Weakness	23%	5.63
Depression/sad mood	20%	6.42
Pruritus	20%	
Dizziness/vertigo	20%	
Loss of concentration	19%	6.12
Numbness/tingling in extremities	16%	
Headaches	11%	6.37
Vision Changes	8%	6.15
Unintentional weight loss		6.38
Daytime sweating		6.35
Loss of sexual desire		6.29

Several symptoms can be directly related to cytokines overproduction:[16-19]

- Fatigue: IL-1, IL-4, IL-6, IL-8, IL-10, TNFa
- Depression: IL-6
- Cytopenia: IL-1, IL-6, TNFa
- Cytokine-induced nerve hyperstimulation: TNFa , IL-1 and IL-6
- Splenomegaly (hematopoietic expansion): TNFa, MIG, HGF, IL-1-RA

This analysis is precious; however, 54% of patients received ruxolitinib. It has been demonstrated that ruxolitinib improves the symptom burden in most patients treated. To better understand the symptoms burden in untreated MF patients, we integrated into the report the following publication:

- Myeloproliferative Neoplasm (MPN) Symptom Assessment Form Total symptom Score: Prospective International Assessment of an Abbreviated Symptom Burden Scoring System Among Patients With MPNs[15]
    - MPN-SAF total symptom score (TSS) -10 has been validated and published in 2017 to provide an expedient, accurate assessment of MPN symptom burden and guide subsequent therapy decisions.
- In this publication, you can see the frequency (incidence) and the mean severity for each of the 10 symptoms kept (Table 2b) and Figure 1 Frequency (a) and severity (b).[15]

Table 2b- Symptoms experienced based on MPN-SAF TSS 10[15]:

Symptom	Incidence	Severity
Fatigue	96%	5
Inactivity	74%	3.1
Early satiety	77%	3.2
Abdominal discomfort	66%	2.5
Night sweats	62%	2.6
Itching	50%	2
Loss of concentration	69%	2.6
Bone pain	52%	2.2
Fever	22%	0.5
Weight loss	42%	1.7
MPN-SAF-TSS		25.3

Figure 1: Symptoms experienced based on MPN-SAF TSS 10[15]

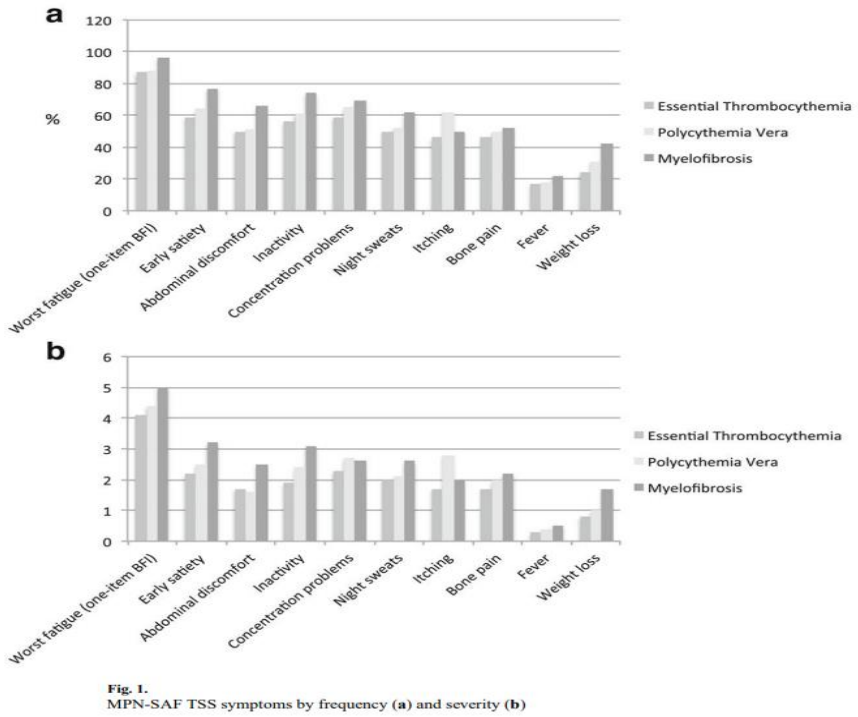


Fig. 1.
MPN-SAF TSS symptoms by frequency (**a**) and severity (**b**)

Myelofibrosis impact on caregivers [1]

- A substantial proportion of patients (40%) reported requiring a caregiver (Table 3). When assessed, myelofibrosis patients who required assistance from a caregiver were significantly higher than those in another disease subtype (58%; P < .001).

Patients classified with high- or intermediate-risk disease were more likely to rely on someone for caregiving (53 and 47%, respectively) than those classified with low-risk.
- Of those who reported requiring a caregiver, 68% stated that a spouse was their primary caregiver, 17% said that it was their son or daughter, and only 1% stated that it was a paid professional.
- Common tasks for which patients required the help of a caregiver included homemaking (61%), companionship (56%), and transportation (50%).
- On average, patients who required a caregiver received help for 12.3 hours in the 7 days preceding the survey.

Table 3 Caregiver requirements*

n (%)	MF (*n* = 174)	PV (*n* = 223)	ET (*n* = 302)	Total (*N* = 699)
Never	73 (42)	148 (66)	201 (67)	422 (60)
Rarely	46 (26)	33 (15)	43 (14)	122 (17)
Sometimes	34 (20)	27 (12)	45 (15)	106 (15)
Often	21 (12)	15 (7)	13 (4)	49 (7)

ET essential thrombocythemia, *MF* myelofibrosis, *PV* polycythemia vera

*Patients were asked, "How often do you rely on someone to assist you with your activities of daily living due to your condition?"

Myelofibrosis impact on employment[1]

- Patients also reported a high impact on the ability to work.
- Only 14% of patients work full-time, and 11% work part-time (Table 1).
- Of all patients (Table 4),
    - 24% reduced hours at work or took a lower-paid job,
    - 12% started receiving disability living allowance
    - 11% took early retirement
    - 8% voluntarily left their job
- On average, over the past 7 days, employed patients with myelofibrosis had missed 4.8 hours of work.
- Of the patients who were employed full-time or part-time at the time of the survey (n = 44), 45% had missed work hours within the past 7 days, and a substantial proportion of patients reported overall impairment at work (mean among currently employed patients (41.4%) and in overall activity (44.9%) (Table 5).

Table 1 – Baseline characteristics including Employment status[1]

Table 1 Baseline characteristics

	MF (n = 174)	PV (n = 223)	ET (n = 302)	Total (N = 699)	P value*
Country breakdown, n (%)					< .01
Australia	5 (3)	4 (2)	1 (0.3)	10 (1)	
Canada	28 (16)	18 (8)	18 (6)	64 (9)	
Germany	57 (33)	50 (22)	42 (14)	149 (21)	
Italy	31 (18)	35 (16)	40 (13)	106 (15)	
Japan	8 (5)	38 (17)	38 (13)	84 (12)	
United Kingdom	45 (26)	78 (35)	163 (54)	286 (41)	
Patient age, mean (range), years	59.6 (28–89)	57.9 (20–85)	54.9 (18–86)	57.0 (18–89)	.035
Sex, n (%)					< .01
Male	89 (51)	118 (53)	98 (32)	305 (44)	
Female	85 (49)	105 (47)	204 (68)	394 (56)	
Disease duration since diagnosis, mean (range), years	4.0 (0–81)	6.6 (0–67)	6.3 (0–33)	–	
Length of time experiencing symptoms before diagnosis, n (%)					.306
< 6 months	56 (32)	56 (25)	96 (32)	208 (30)	
6–12 months	48 (28)	51 (23)	71 (24)	170 (24)	
1–2 years	32 (18)	47 (21)	54 (18)	133 (19)	
> 2 years	38 (22)	69 (31)	81 (27)	188 (27)	
Patient-reported prognostic risk score, n (%)					
High risk	23 (13)	20 (9)	60 (20)	103 (15)	
Intermediate risk	50 (29)	27 (12)	48 (16)	125 (18)	
Low risk	26 (15)	57 (26)	67 (22)	150 (21)	
Not known	75 (43)	119 (53)	127 (42)	321 (46)	
Employment status, n (%)					< .01
Employed full time	24 (14)	63 (28)	86 (28)	173 (25)	
Employed part time	20 (11)	23 (10)	59 (20)	102 (15)	
Unemployed, seeking employment	1 (1)	3 (1)	4 (1)	8 (1)	
Unemployed, not seeking employment	6 (3)	2 (1)	5 (2)	13 (2)	
Retired	75 (43)	75 (34)	84 (28)	234 (33)	
Self-employed	14 (8)	26 (12)	27 (9)	67 (10)	
Homemaker	8 (5)	16 (7)	17 (6)	41 (6)	
Student	2 (1)	2 (1)	3 (1)	7 (1)	
Disability	13 (7)	8 (4)	9 (3)	30 (4)	
Sick leave	5 (3)	3 (1)	6 (2)	14 (2)	
Other	6 (3)	2 (1)	2 (1)	10 (1)	

Table 4 Impact of MPN on work[1]

Table 4 Impact of MPN on work*

n (%)	MF (n = 174)	PV (n = 223)	ET (n = 302)	Total (N = 699)
Reduced hours at work	36 (21)	33 (15)	70 (23)	139 (20)
Voluntarily terminated your job	14 (8)	14 (6)	35 (12)	63 (9)
Been involuntarily terminated from job	3 (2)	7 (3)	4 (1)	14 (2)
Gone on disability living allowance	21 (12)	9 (4)	21 (7)	51 (7)
Taken early retirement	19 (11)	12 (5)	27 (9)	58 (8)
Taken a lower paid job	5 (3)	8 (4)	20 (7)	33 (5)

ET essential thrombocythemia, *MF* myelofibrosis, *MPN* myeloproliferative neoplasms, *PV* polycythemia vera

*Patients were asked, "As a result of your condition, have you ever . . ." Percentages represent those who responded "Yes"

Table 5: Work and activity impairment[1]

Table 5 Work and activity impairment

All patients	MF (n = 174)	PV (n = 223)	ET (n = 302)	Total (N = 699)
Overall activity impairment	44.9	40.3	36.3	39.7
Employed patients	MF (n = 44)	PV (n = 86)	ET (n = 145)	Total (n = 275)
Absenteeism	11.7	5.9	7.4	7.6
Presenteeism (i.e., working while sick)	35.2	29.6*	30.7†	31.1
Overall work impairment	41.4	33.0*	35.7†	35.8
Hours missed from work, n (%)				
Mean, hours‡	4.8	3.3	2.6	3.1
SD	3.71	17.25	6.52	10.27
1–3 h	4 (9)	8 (9)	18 (12)	30 (11)
4–6 h	8 (18)	9 (10)	9 (6)	26 (9)
7–9 h	3 (7)	4 (5)	14 (10)	21 (8)
> 10 h	5 (11)	6 (7)	7 (5)	18 (7)

ET essential thrombocythemia, *MF* myelofibrosis, *PV* polycythemia vera

*n = 83

†n = 140

‡Mean scores calculated using Work Productivity and Activity Impairment scoring (http://www.reillyassociates.net/WPAI_Scoring.html)

4. Experiences with Currently Available Treatments

The development and commercialization of JAK inhibitors (JAKi) revolutionized the treatment of this neoplasia.

Currently, the FDA has approved a total of four JAKi:

- Jakafi –(ruxolitinib) 2011
- Inrebic (Fedratinib) in 2019
- Vonjo (pacritinib) in 2022
- Ojjaara (Momelotinib) in 2023

Only two JAKi are currently available in Canada:

- Jakafi –(ruxolitinib) 2012
- Inrebic (Fedratinib) in 2023

JAKis are mostly perceived by HCPs as medications that alleviate symptoms and improve patient QoL, which aligns with their primary treatment goal.

However, JAKi is a targeted therapy that reduces abnormal stem cell activation and cytokine overproduction. JAKi indeed improves symptoms in most patients by directly decreasing the level of cytokines and reducing the spleen volume.

For obscure reasons, the medical community does not consider JAKi, a disease modifier class of treatments. During the last decade, it became undeniable that JAKi prolongs survival despite the ethical design of phase III clinical trials, which allows cross-over after 24 weeks.[8-12] Several exploratory analyses demonstrated the capability of ruxolitinib to

improve fibrosis status and normalize bone marrow cellularity in a significant proportion of patients.[7] Even the variant allele frequency (VAF) can be reduced significantly under the treatment of a Jak inhibitor.

In 2016, five years after the commercialization of ruxolitinib and at least four years after the publication of survival benefits observed in COMFORT-1 and COMFORT-2, the most prevalent treatment objectives for physicians were the reduction of symptoms and better quality of life. Only 43% of HCPs have mentioned slow/delayed progression as one of their top three treatment objectives, while it is more prevalent in patients.[1]

This misperception of JAKi might be explained by several factors involving clinical practice and clinical trial design. HCPs who treat myelofibrosis also treat CML, and their perception might be biased by the clinical response obtained with BCR: ABL TKI in CML. After discussing this with several HCPs, it became evident that this element influenced their mindset. However, several differences are observed between the clinical practice in CML and myelofibrosis:

- HCPs initiate the treatment immediately after CML diagnosis; they do not wait for symptoms or cytopenia to progress like for myelofibrosis. Even the most potent BCR-ABL TKI cannot induce an adequate and prolonged response in advanced CML patients.
- HCPs can regularly track clinical response by PCR in CML, which is not done for myelofibrosis.
    - Unlike CML, where all patients have the BCR-ABL gene, the molecular abnormality varies in myelofibrosis, discouraging the establishment of routine clinical molecular tests to track clinical progression.
- For HCPs, the primary treatment goal in CML is to reduce translocated load and avoid disease progression, while for myelofibrosis, the goal is to reduce the burden of symptoms.[1] HCPs seem to have a palliative mindset when approaching this patient population.

More recently, the medical community has debated the ideal clinical endpoints for assessing new treatment efficiency in myelofibrosis.

- **TSS50% - Symptoms** are considered as a soft and subjective endpoint. Our interviews with HCPs revealed that most HCPs are reluctant to use validated symptom scores developed and used in all JAKi clinical trials. This aspect is also collaborated by the landmark survey, where less than 25% of HCPs use the validated MPN-SAF TSS (MPN10) symptoms score to conduct symptoms evaluation[1].

- **SVR35% / Spleen volume** is reliable and easy for patients compared to BM assessment. In clinical practice, spleen palpation is used instead of MRI. Both techniques seem reliable. However, our interviews with HCPs revealed they are comfortable with big spleens, so, in their mind, reducing their volume does not translate into a significant clinical benefit, despite its evident involvement in symptoms burden and cytopenia progression. This aspect is also collaborated by the landmark survey, where only 38% of HCPs mentioned reduction of the spleen as one of the three top treatment objectives.[1]

- **BM biopsy – Fibrosis rate assessment**
  - BM biopsy is an invasive procedure, and most patients are reluctant to have it performed as a follow-up. Our interview with HCPs corroborates this fact. Moreover, HCPs try to avoid participating in clinical trials that require this type of procedure as much as possible.
  - BM fibrosis analyses weren't standardized during the 1st clinical trials, and the rarity of the disease makes pathological reading less uniform. In the future, AI may improve non-MPN expert centers' capability to assess fibrosis more uniformly and by WHO standards.
  - Due to the heterogenicity of the BM infiltration, it is also difficult to guarantee the representativity of the sample taken and analyzed.
  - Variant allele frequency could be interesting. However, three tests must be developed: JAK2, CALR, and MPL. CALR was not even identified during the enrollment of COMFORT-1 and COMFORT-II. To our knowledge, these techniques have not yet been developed for routine assessment.

Patient perspectives about current clinical practices:

- The minimization of JAKi's impact on disease progression, the palliative treatment approach, and the debate around clinical endpoints reinforce the patient perspective that the medical community does not fully understand the disease.
- Patient's fear that HCP perception regarding myelofibrosis (an indolent disorder) reduces the urgency to treat with adequate treatment (e.g. JAKi).
  - 89% of MPN patients worry that their condition will get worse.[1]
  - Patients wish more frequently than HCPs to slow/delay disease progression (58% vs 43%).[1]
  - Patients wish more frequently than HCPs to have healthy blood count (38% vs 10%).[1]

- Because JAKi is perceived by HCPs as a symptom treatment that induces cytopenia, and cytopenia such as anemia is linked with a poor prognosis, JAKi introduction is delayed as much as possible, limiting its benefits and impact on survival.
- Compared to CML,
    - The patient community needs to work harder to access mutation testing and to get their symptoms appropriately assessed.
        - In the landmark survey, 43% of patients didn't know their risk score.[1]
        - Moreover, less than 25% of HCPs use the validated MPN-SAF TSS (MPN10) symptom score to evaluate symptoms, reducing the overall symptoms assessment. By not using a validated tool, patients might forget or not realize that one symptom is associated with the disease instead of just getting older.[1]
        - 59% of MPN patients mentioned that they often feel worse than my physician is aware of.[1]

These observations have been corroborated with HCPs and patient interviews. These observations are dramatic for patients who depend on their risk score and symptom burden to access appropriate medication.

- The patient community needs to work harder to access available treatments. Their treatment is often initiated too late when their cytopenia is too advanced, limiting the dosage of available options. Most patients are treated with a suboptimal dose of ruxolitinib, missing the full potential observed in clinical trials (ASH 2023).

Myelofibrosis is more complex than CML, and the disease progression involves more molecular processes than CML. However, even if JAKi can not provide a perfect response like most BCR-ABL TKIs for 95% of patients, Jakavi demonstrated an improvement of the BM fibrosis in 35% of patient evaluated and a clinical response regarding the BM fibrosis (stabilization and improvement) of 76% of patients evaluated after five years of treatment. Jakavi also demonstrated statistically significant survival benefits. These results are seen in other hematological malignancies, and the treatment inducing that type of response is considered effective, not just a symptom medication.
The minimization of 1) the severity of the disease and 2) the clinical benefits of JAKis gravely impact patient access in a timely fashion. This situation significantly reduces the ability to achieve the best clinical response possible for these patients.

Fatigue, Anemia and blood transfusion in myelofibrosis

Anemia

Anemia and RBC transfusion dependence constitute key adverse prognostic factors in MF that are inversely associated with quality of life[29,30] and survival.[31,32] The risk of death was 1.5-fold higher in severely anemic, transfusion-dependent MF patients compared to that in moderately anemic patients. [33] Anemia is a prime correlate of progressive disease in MF patients; consequently, MF-related anemia, especially transfusion-requiring anemia, is one of the most important disease consequences to address. A stratification study of 1,109 patients by grade of anemia demonstrated that patients with severe (Hb < 8 g/dL or transfusion dependence) and moderate (Hb in the range 8–10 g/dL) anemia had a median survival of 2.1 and 3.4 years, respectively.[33]

Why blood transfusions don't work properly

Fatigue is frequently linked to anemia; blood transfusion (RBCT) to increase hemoglobin (Hg) levels could be a treatment option. The expected clinical outcome for RBCT in cancer patients is improved symptoms of anemia and QoL. The assumption is that elevating Hg concentration closer to physiologic values improves symptoms of anemia and, subsequently, QoL. However, a clear correlation between Hg levels and fatigue can not always observed.[20] As discussed earlier, fatigue experienced by myelofibrosis patients is mainly driven by the overproduction of cytokines (IL-1, IL-4, IL-6, IL-8, IL-10, TNFa). So, the lack of correlation between Hg levels and fatigue makes more sense.

The pathophysiology of fatigue involves neuroendocrine dysregulation, alteration of cellular immunity and abnormal inflammation caused by gene dysregulation. Cytokines such as IL-6, IL-1 and TNF-a have been associated with fatigue.[21] MF patients are often cachectic, and like in other cancers such as acute leukemia, the cachectic process weakens muscles, reducing nutriment dysregulation and exacerbating inflammation due to GI toxicity (Gut-muscle axis). [22]

In MDS, another myeloid cancer, the RBC-ENHANCED study has demonstrated that despite RBCT, patients can experience a decline in their scores (symptoms/functional). This observation underscores the complex interplay of factors contributing to QoL in patients, such as frailty, comorbidity, disability, and disease-related inflammation. [23] So, for myelofibrosis patients in the era of JAKi, RBCT treatment utility is limited to reducing the risk of bleeding by increasing Hg when it is too low.

The financial cost of RBCT

In 2018 publication from UHN Foundation, it was suggested that each unit costs roughly $650 to $1,550 to deliver from the donor to the patient. Considering the average cost of

The real cost of RBCT for patients and their caregivers
This section will find the Heal Canada Online survey results: Impact of frequent transfusion on patients QoL- 2024 (n=24).

Rationale:
Several medical publications mention that blood transfusions significantly impact patients' QoL. The patient interview corroborates this statement. However, we could not find enough evidence in the literature. So, Heal Canada launched an online survey to address this topic in 2024.

Demographic:
- 100% Canadian
- 50-50 Male-female
- ≥ 35 years old

Responses:
1) Patients received RBCT for the following reasons (more than one response could be selected):
   - Fatigue - 75%
   - Anemia – 75%
   - Hg too low- 75%
2) Most patients received RBCT every week or every two weeks for several years (mostly between 2 to 5 years)
3) It takes an average of 5.5 hours to receive an RBCT
4) Most patients must drive an hour or less to receive their transfusion. However, 25% of respondents said driving takes around 4 hours to receive their RBCT.

Based on 2, 3, and 4, it takes 6.5 to 9.5 hours to receive a blood transfusion every week or every two weeks.

5) 75% of responders had mentioned experiencing adverse reactions during the RBCT (more than one response could be selected):
   a. Fatigue (50%)
   b. Blood pressure drop (25%)
   c. Allergic reactions (25%)
6) 75% of responders had mentioned experiencing adverse reactions after a RBCT are (more than one response could be selected):
   a. Restless leg syndrome – 75%
   b. Reduced daily living and functional capabilities (50%)

   c. Emotional and mental health issues (anxiety, depression) 50%
   d. Fatigue – 50%
   e. Pain, body aches or severe pain – 50%
7) 100% of respondents mentioned that the benefits of RBCT wear off before the next RBCT.
8) Only 75% of the patients received medication for iron overload.
9) 25% of responders need caregivers with them to receive their RBCT
10) The level of stress regarding their RBCT is at 75% / 0, being not stressful at all to 100% (very stressful)
11) The impact on QoL is 86% / 0 being no impact at all to 100% (significant impact)
12) The impact of RBCT on their mental and emotional well-being is 89% / 0 being no impact at all to 100% (significant impact)
13) The impact of RBCT on their social activities is 83% / 0, being no impact at all to 100% (significant impact)
14) 100% of responders experienced challenges due to their RBCT (more than one response could be selected):
   a. Mental Health -100%
   b. Family reponsabilities – 75%
   c. Work-life balance – 75%
   d. Having a good QoL – 75%
   e. Transportation – 25%
   f. Housing responsibilities – 25%
   g. Budget struggles – 25%
   h. Work Challenges – 25%
   i. Other – Stress associated with not knowing whether a transfusion is needed. 25%
15) 50% of responders mentioned that receiving regular RBCT impacted their working status.
16) 50% of responders mentioned that receiving regular RBCT impacted their caregiver's working status.

Current treatment limitations:

Anemia is present in approximately a third of patients at diagnosis, eventually developing in nearly all patients. The need for RBCT is an independent adverse risk factor for both overall survival and leukemic transformation.

In patients, disease-related anemia can be exacerbated by treatment with ruxolitinib because of myelosuppression, an adverse event that is consistent with the drug's interference with erythropoietin signalling via JAK-STAT (especially JAK2), which is essential for erythropoiesis.[34]

Ruxolitinib

COMFORT-I & 2 pooled 3-year data showed ruxolitinib dose-dependent anemia: anemia worsened in 69% of the patients with baseline anemia (< 10 mg/dL) and 61% of the patients who did not have baseline anemia experienced on-treatment anemia.[35] Even if this analysis has demonstrated that ruxolitinib-induced anemia did not decrease overall survival, [36] a more conservative ruxolitinib dosing regimen has become common practice. This dose reduction is impacting the spleen response, the improvement of symptoms and survival.[37]

Fedratinib

Fedratinib induces similar myelosuppression to ruxolitinib because it also interferes with erythropoietin signalling via JAK-STAT. In the phase 3 JAKARTA trial, in which JAK-inhibitor-naïve myelofibrosis patients were treated with fedratinib, anemia was the most common hematological toxicity; 34% and 75% of the patients developed new or worsening grade 3 anemia at a median of 2 and 3 months after treatment initiation, respectively, and 17% of the patients became transfusion-dependent during treatment.[38]

In the JAKARTA-2 trial, which included patients previously treated with ruxolitinib, 53% had Hb < 10 g/dL, and 14% were transfusion-dependent at baseline. Grade 3/4 anemia was the most common hematological adverse event (38 to44%).[38,39]

Our interview with Canadian HCPs confirmed that anemia is a preoccupation for them. HCPs can be reluctant to prescribe JAKi if the patients have low hemoglobin levels because, as already discussed, anemia and blood transfusions impact survival and patients' quality of life. Also, to minimize secondary effects, HCPs tend to use a smaller dose of Jakavi, affecting the treatment efficacy.

ACVR1 can address limitations specific to ruxolitinib and fedratinib for anemic myelofibrosis patients.

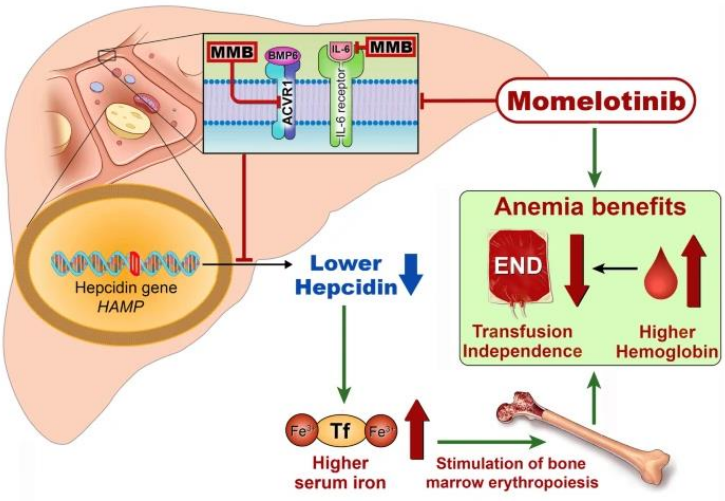
5. Improved Outcomes

Myelofibrosis is a cancer associated with a high disease burden, reduced QoL and shortened survival. Anemia is frequent in these patients and can limits seriously their treatment options. RBCT is inefficient in addressing fatigue in these patients and burdens their QoL tremendously. Frequent RBCT induce iron overload, which impacts hematopoiesis and affects their survival. JAKi is the only effective treatment currently to address the physiopathology of myelofibrosis.

Like other JAKi, momelotinib provides a significant clinical spleen and symptom response. However, momelotinib can be prescribed at the approved dose for anemic patients, maximizing the treatment efficacy.

Momelotinib has unique inhibitory activity on the BMP6/ACVR1/SMAD and IL-6/JAK/STAT3 pathways, resulting in decreased hepcidin (master iron regulator) expression, higher serum iron and hemoglobin levels and restored erythropoiesis (Figure 2).

Figure 2: Momelotinib mechanism of action



Clinical data on momelotinib from the phase 2 and the two phase 3 SIMPLIFY trials consistently demonstrated high rates of sustained transfusion independence. In a recent phase 2 translational study, 41% of the patients achieved transfusion independence for ≥ 12

weeks. In the phase 3 trials SIMPLIFY-1 and SIMPLIFY-2, 17% more JAK inhibitor-naïve patients and two-fold more JAK inhibitor-treated patients achieved or maintained transfusion independence with momelotinib versus ruxolitinib and best available therapy (89% ruxolitinib).

6. Experience With Drug Under Review

Based on comments from patients who used it in the USA, most patients have improved Hg and reduced transfusion needs, which is encouraging for them. This aspect of the treatment is mentioned in more than 70% of the comments. One patient could delay his transplantation due to the response on Ojjaara.

The medication seems well-tolerated overall (~ 65% of comments). Some individuals experience adverse events such as headaches, pain, fatigue, and GI issues and do better after a month. A small portion of patients have their doses reduced to 150mg and 100mg. However, a minority of patients mentioned they had to stop due to AEs or progression to MDS or AML.

Here are some of their quotes:

"My hemoglobin has touched over into normal range for the first time in ages" I am thrilled.

"Ojjaara has been a God send for my life. Went from needing transfusion every two weeks to 6 to 8 weeks."

"I started two months and a half ago, and sometimes I feel dizzy and have nausea, but I feel better than on ruxolitinib, and I don't need transfusion every month. My life is better now."

"I was miserable on Ojjaara; come off back on Jakafi."

Several mentioned that patients' experiences can vary, and it is important to feel they have options after ruxolitinib and fedratinib.

7. Companion Diagnostic Test

- To our knowledge there is no companion diagnostic test necessary to use momelotinib versus another JAKi.

8. Anything Else?

Conclusion

- Transfusion-requiring anemia is a tremendous burden for patients and healthcare systems:
  - RBCT tremendously impacts patient QoL and patient/caregiver productivity.
  - RBCT is inefficient in addressing myelofibrosis patient fatigue.
  - RBCT should be reserved for conditions treated only with RBC units.
- Anemic patients won't benefit from ruxolitinib, as demonstrated by the clinical trial, due to the conservative dosing strategy.
- Momelotinib is the only clinical alternative for anemic myelofibrosis patients.
- Access to momelotinib in the frontline setting can change the lives of anemic myelofibrosis patients.
- Access to momelotinib in the second-line setting can change the life of anemic myelofibrosis patients.
- Canadian anemic myelofibrosis patients need this third JAKi option to slow and delay the progression of their disease as well as to improve their QoL.

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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 help from outside the organization has been provided to support this submission.

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.
   - No help from outside the organization has been provided to collect or analyze the data used in this submission.

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.
   - See the list of pharmaceutical companies providing funding to support Heal Canada.
     - i None of these companies has a direct or indirect interest in the drug submission.
       - Novartis, Canada
       - Servier, Canada
       - SOBI, USA

Table 1: Financial Disclosures

Check the 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	Over $50,000
Novartis			$20,000	
Sobi US			$20,000	
Servier	$2,500			

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,Ph.D
Position: Chief Scientific Officer
Patient Group: Heal Canada
Date: 04-07-2024

CADTH Reimbursement Review
Patient Input Template

Patient Input Template for CADTH Reimbursement Reviews

Name of Drug: momelotinib (Ojjaara)

Indication: For the treatment of disease-related splenomegaly or symptoms, and anemia in adult patients with primary myelofibrosis, post polycythemia vera myelofibrosis or post essential thrombocythemia myelofibrosis who are Janus Kinase (JAK) inhibitor naive or have been treated with a JAK inhibitor

Name of Patient Group: The Leukemia & Lymphoma Society of Canada (LLSC) and The Canadian MPN Network (CMPNN)

Author of Submission: Colleen McMillan, Advocacy Lead, 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 MPN Network - canadianMPNnetwork.ca

The Canadian MPN Network (CMPNN) was founded in 2014 as an organization connecting and helping Canadians from coast to coast to coast who are dealing with the challenges of living with a myeloproliferative neoplasm (MPN). The CMPNN is led by a volunteer cross-Canada Board of Directors composed primarily of MPN patients who meet virtually. The Board has a “patient first” mindset and is dedicated to improving the quality of life for Canadian MPN patients by providing education, advocacy, and support. CMPNN initiatives are free of charge to Canadian MPN patients and their care partners and include the annual conference, a comprehensive website citing relevant, factual, knowledge-based information and resources, linkages to the medical community, 1-on-1 support, and active regional support groups.

MISSION: Through Education, advocacy and support, the Canadian MPN Network strives to improve the quality of life for Canadian MPN patients and their support network.

2. Information Gathering

Three online surveys were created, and information was gathered between March-May 2024. Surveys #1 and #2 were developed by The CMPNN and were distributed by both CMPNN and LLSC. Survey #3 was developed and distributed by both The CMPNN and LLSC. All surveys were in the English language only.

Survey #1 – This survey asked for input from patients and caregivers who have lived experience with Myelofibrosis. The survey was shared through various social media channels and throughout the Canadian MPN Network regional support groups. There were 33 respondents to this survey.

Survey #2 – This survey was intended to gather patient experience with the drug under review, momelotinib. The survey was shared through various social media channels and throughout the Canadian MPN Network regional support groups. Responses were received from Canadian Patients as well as Patients from the United States of America and Germany. There were 11 respondents to this survey.

Survey #3 – This 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 myelofibrosis. There were 29 respondents to this survey.

In survey #3 respondents were asked if they had recently completed a survey issued by the Canadian MPN Network regarding myelofibrosis or momelotinib. 1 respondent answered “yes” and was disqualified from the survey.

The majority of respondents (70.37%) indicated that they were the myelofibrosis patient (past or present). 25.93% of respondents indicated that they were a caregiver of a myelofibrosis patient (past or present). One respondent answered “other” and was disqualified from the survey.

4 respondents answered that their myelofibrosis (MF) was not classified as intermediate or high-risk. These respondents were disqualified from the survey.

All respondents indicated that they lived within Canada.

LLSC also conducted two 1 on 1 interviews with patients currently living with myelofibrosis and being treated with momelotinib.

3. Disease Experience

Many myelofibrosis (MF) patients often rely heavily on caregiver support to navigate daily life and manage their symptoms. Tasks such as meal preparation, shopping, and household chores can become difficult, or impossible for patients, placing a significant burden on both patients and their caregivers. The physical, emotional, and financial toll of dealing with MF profoundly impacts the lives of patients and caregivers alike.

Survey respondents were asked do/did you require caregiver support to manage your MF symptoms?
8/20 (40%) answered - Yes

Patients described specific tasks of daily living they now depend on caregivers for, ranging from basic daily activities to more complex needs such as driving and medication management:

- “Dependent on caregiver for most meals, shopping, housework”
- “Weakness, incontinence, activities of daily living. Requires assistance with all aspects including driving”
- “Caregiver was mandatory”
- “Driving, remembering to take pills, cooking, cleaning”
- “Requires assistance with daily activities such as bathing, groceries, house cleaning”
- “Unable to do a lot of everyday chores for myself or put them off indefinitely”
- ”Some tasks, deep cleaning and yard work I have to pay someone to do for me”

Witnessing the decline in a loved one's health and daily functioning causes substantial stress and anxiety for caregivers. Themes emerging from respondents' answers highlight the emotional strain and practical challenges caregivers face. For instance, caregivers’ worry and concern over their partner's condition, financial strain, and the demanding nature of caregiving duties. Caregivers’ own activities also become restricted due to their loved ones’ MF, impacting their quality of life.

Patients elaborated on the broader effects of MF on their caregivers, noting concerns about the future, and the emotional toll of witnessing their partner's illness. These insights underscore the profound impacts of MF on both patients and their caregivers.

- “Worried and concerned, causing undue stress and panic to my partner”
- “Creates a burden for my care partner, financially”
- “My wife is my care partner and so far, it has been a full-time job. We are at the bone marrow clinic a minimum 3 times per week. Then the trips to Foothills ER, fetching drugs, the cooking etc.”
- “I’m in a wheelchair and rely on my husband for heavy cleaning and taking care of grocery shopping and other things which involve getting out of the house, such as appointments etc. I find I do not try to get out as much because of the necessity of having to load a wheelchair and walker in the car which involves lifting which is hard on him. A lot of worry about how the symptoms are affecting my husband.”
- “Limits his activities as well like travel, socialization”
- “My MF has caused my partner to have great worry about the future. Everything is very unknown. We don't know what time we might have left to enjoy retirement, travel, and to spend time with our teen and young adult children”

- “The partner has a limited quality of life due to consideration for the sick person”
- “Well, I got divorced, so perhaps a large impact”

The symptoms associated with MF are diverse, and their impact can vary widely in type and severity. Patients commonly experience fatigue, anemia, and weight loss. An enlarged spleen is also prevalent, which can sometimes impair the patient’s ability to eat and maintain adequate nutrition. These symptoms collectively contribute to the challenging and multifaceted nature of managing MF.

Survey respondents were asked to identify which side effects of MF had the most effect on them. 20 respondents answered this question. The chart below reflects their responses.

ANSWER CHOICES	RESPONSES	
Fatigue	95.00%	19
Enlarged spleen	75.00%	15
Anemia (low red blood cell counts)	70.00%	14
Night Sweats	45.00%	9
Bone/joint pain	40.00%	8
Early satiety (getting full quickly at mealtimes)	35.00%	7
Brain fog	35.00%	7
Weight loss	35.00%	7
Itching/Pruritus	25.00%	5
Gout	15.00%	3
Frequent infections	15.00%	3
Total Respondents: 20		

Some respondents described in more detail, the impacts of MF, affecting their quality of life:

- “Diarrhea, nausea, vomiting and extreme fatigue”
- “I’m tired, fatigued most of the time. I get very painful deep bone pain. My spleen still feels uncomfortable a lot of the time even though it’s shrunk 5mm. I get an itch once in a while that feels like there is something crawling underneath my skin”
- “Fatigue, breathlessness, frequent insomnia, bone pain relieved by Magnesium”
- “Headaches, fatigue, shortness of breath on exertion”
- “My energy level is slightly lower. I have had a number of bleeding incidents - nosebleeds as well as abdominal hemorrhaging”
- “Feel less productive, take many medications with side effects which decreases QOL”
- “Throughout the day, not too bad, but after supper and through the night, a lot of bone pain and cramping in the legs and feet. Not able to walk too far and tires easily. Brain fog and memory problems. Blood work and transfusions every week. Skin really thin, bruises and cuts easily”
- “Extreme fatigue, bone pain, nausea, brain fog. At times it feels completely debilitating. It seems like my doctors don’t really understand or care. I feel unsupported”
- “The fatigue, bone pain or what I describe as feeling like my veins and arteries are on fire. Severe itching. All of this makes me feel like I am dragging through the day. I work in an office and it’s hard to

focus sometimes and I'm late every morning. I can't take a normal shower otherwise I will be screaming for a couple hours afterwards and getting dressed is also hard for that reason. gabapentin just takes the edge off so that I can function. It's impossible for me to commit to any social events. Sometimes just going to a family members home is too much. I just don't feel like doing much. So, my family and friends have become distant for sure. My quality of life is very, very poor due to all I've described."

The symptoms of MF, whether physical or mental, can be highly debilitating. MF often hinders patients and caregivers from maintaining their usual work or daily routines, sometimes making it impossible to do so. This not only imposes a financial strain but also significantly affects their mental well-being, as demonstrated through respondents' answers below.

Respondents were asked, what impact, if any, did MF treatment have on the patient's or caregiver's ability to continue with normal routines and future plans? (example – work, travel, etc.)?
20 respondents answered this question. Responses are reflected in the chart below.

ANSWER CHOICES	RESPONSES	
Significant change	80.00%	16
Minor change	10.00%	2
No change	10.00%	2
TOTAL		20

Respondents elaborated on the affects that MF had on their or their caregivers' ability to work and maintain regular routines…

- "Full time work was hard to manage"
- "Not possible to work. Not possible to travel. Not possible gather with groups of friends and family"
- "Need for frequent bloodwork to manage disease"
- "No work for many months"
- "I've been off of work on disability for over a year now, I'm constantly fighting fatigue. If I overdo it my body crashes. Plus, my bone pain has affected my ability to get a good sleep."

Respondents were asked, “did you or your caregiver(s) experience a loss of income due to MF treatment?

11/20 (55%) answered - Yes

Some respondents also commented about loss of income, and/or additional expenses due to MF:

- “Had to quit working due to fatigue and low energy”
- “Information is not publicly available to know where and who to ask about MF and there are no benefits in place for caregiver who is not paid for her services”
- “When having to get phlebotomies they only do them during weekdays. No evenings or weekends. I have to pay ridiculous fees to park around the hospital. When I have Dr appointments, I usually have to take half a day off of work because the labs are usually busy, so you have to do blood work an hour before hand and you have a 2 hour wait just to get blood drawn. Then it takes another 30 to 45 minutes for the results to get entered into the system for the Dr to see.
- “I had to go on disability a few months after diagnosis, too emotional to continue career”
- “My caregiver has to take unpaid leave from work if I need help with appointments”
- “I had to retire from my career very early. Full responsibility for earning on my partner”

Living with myelofibrosis (MF) brings significant mental exhaustion for both patients and caregivers. The fear of the unknown, anxiety about the future and the possibility of disease progression, a decline in quality of life, and the inability to perform daily activities as before are major contributors to this mental burden. These challenges affect not only patients but also those who care for them, amplifying the emotional toll of managing MF on both fronts.

Respondents were asked, Overall, what kind of impact would you say MF has had on the **mental health status** of the patient and/or caregivers?

13/20 (65%) answered - negative to extremely negative impact

- “Very taxing mentally and physically for myself as the caregiver”
- “Mentally drained worrying about health”
- “Emotionally/psychologically crushed, could not continue my engineering career”
- “Anxiety”

One respondent simply, but powerfully, commented one word - “Shattered”

Respondents were asked, what kind of impact has MF had on your **personal life/home life**?

17/20 (85%) answered - negative to extremely negative impact

- “Not enough energy to live a full life”
- “Accessibility. Emotional impact. Intimacy. Family relationships. Financial”
- “Very uninterested in any pleasures I enjoyed in the past. Shopping and keeping my house as clean and tidy as I used to because of lack of energy and because I get short of breath.”
- “Tend to need mid-afternoon rests of varying times.”
- “Need to be positive by nature can be a challenge.”
- “As caregiver, it takes up all my free time. Also, I'm the driver to and from appointments, prescriptions, hospitals. There are no benefits in place for someone who’s in my position and the work I do.”
- “Ended my Marriage. My children have been affected and are always worried when I get sick if they are going to lose me”

Respondents were asked, what kind of impact has MF had on your **social life**?

17/20 (85%) answered - negative to extremely negative impact

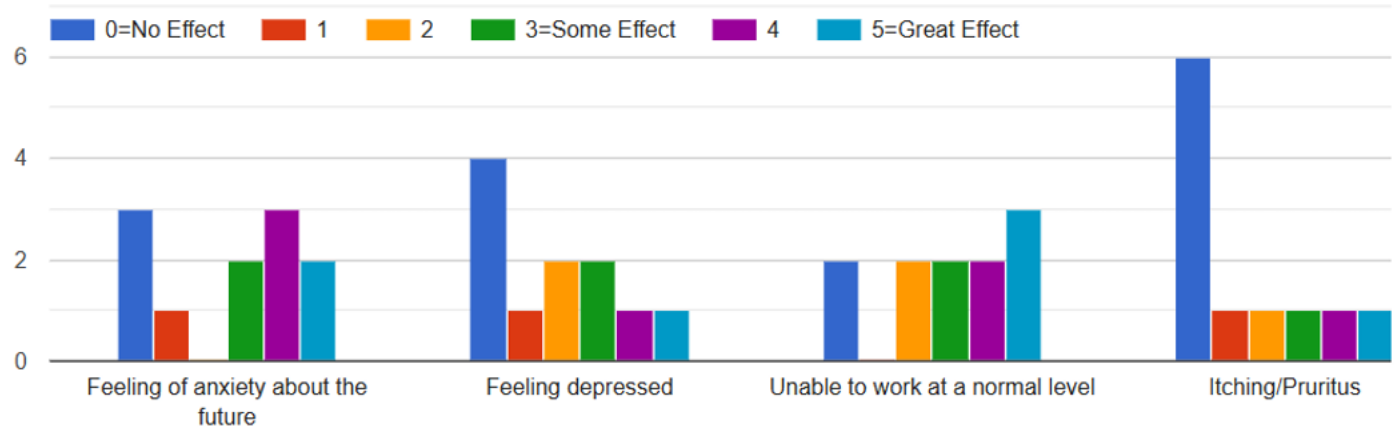
- “Stigma. Weakness. Accessibility, wheelchair transport etc.”
- “Trying to not let it impact me although I have pulled back a bit. Being cautious with wearing a mask is a good thing after a bad flu/cold that lasted for many weeks.”
- “The diagnosis amplified the need to isolate with covid. Socially, we still don't see people when there will be a large crowd... can be isolating”
- “No free time for myself as the caregiver and for the patient she feels alone, alienated, left out”

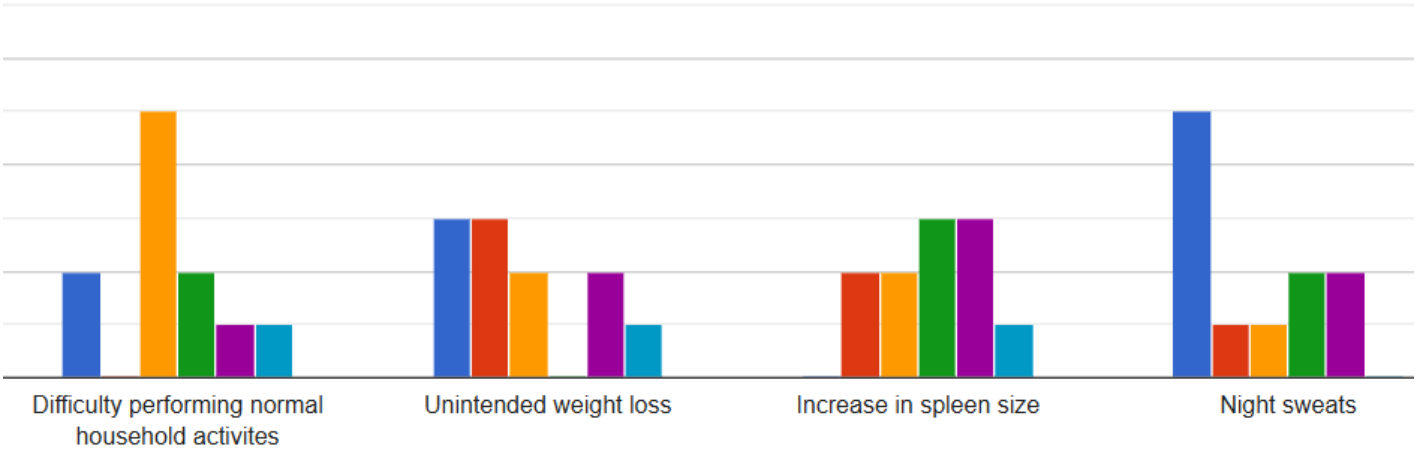
Respondents who answered that MF has had a negative impact on these areas of their lives were asked, what factors contributed to these negative impacts? Answers are reflected in the chart below.

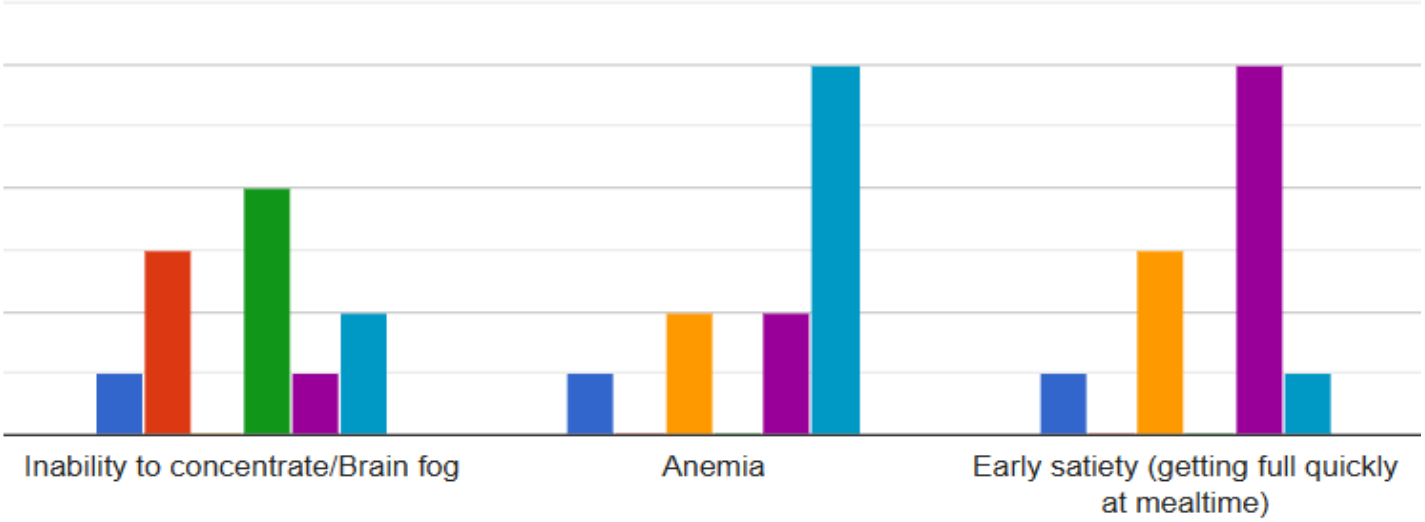
ANSWER CHOICES	RESPONSES	
Low energy	88.89%	16
MF symptom burden	61.11%	11
Depression and anxiety	50.00%	9
Fear of infections	44.44%	8
Frequent hospital visits	33.33%	6
Total Respondents: 18		

In survey #2, respondents were asked to rate the impact of various effects of MF. Responses are reflected in the charts below:

Rate from 0 to 5 the degree to which each of the following affected you prior to taking Momelotinib **with 5 being the most impactful.**

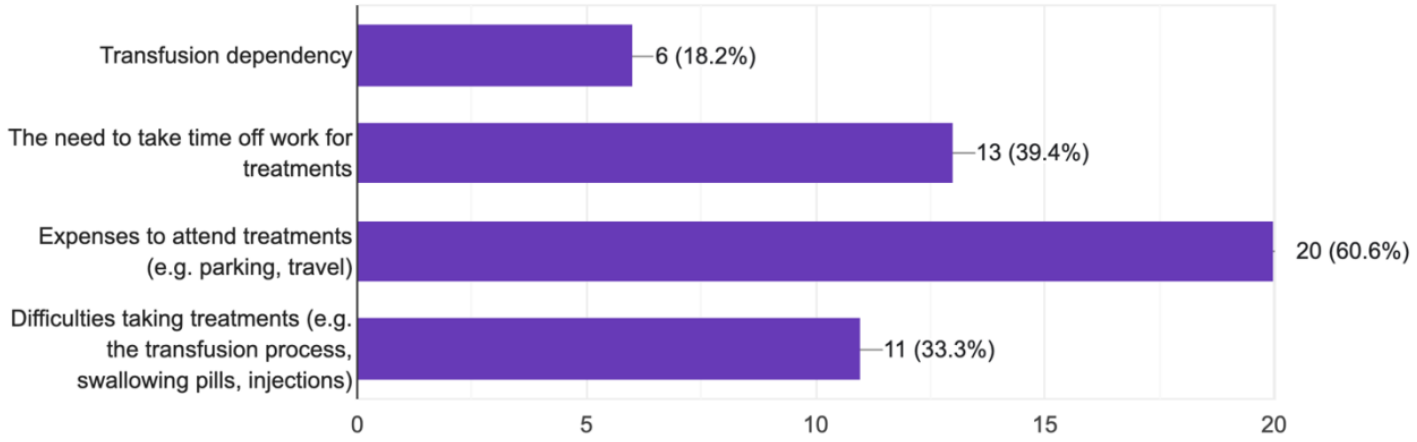






Indicate which of the following has had an impact on you as a patient.

33 responses



4. Experiences With Currently Available Treatments

While treatment options for myelofibrosis (MF) exist, they often have significant limitations and burdensome side effects that necessitate additional healthcare resources. These current treatments leave considerable gaps and unmet needs among patients, as they may not offer sustained symptom relief or effectively address the underlying causes of the disease.

Respondents were asked to select which treatment(s) they have taken for MF (other than momelotinib)

None
ruxolitinib (Jakavi)
inrebic
Transfusions
Epoetin
Urea Apixaban
Pantoprazole
Hydroxyurea
Watch and Wait
Surgery (e.g. spleen removal)
Radiation
Immunotherapy
Stem cell transplant

One respondent left a comment – “Jakavi was only taken for 3 weeks last year because the hemoglobin dropped sharply”

Respondents were asked to select the TOP 5 side effects of MF treatment that affected them the most. Responses are reflected in the chart below:

ANSWER CHOICES		RESPONSES	
Fatigue		60.00%	12
Weight loss		40.00%	8
Thrombocytopenia: Low platelet count		40.00%	8
Frequent Infections		35.00%	7
Abdominal pain		30.00%	6
Other (please specify)	Responses	30.00%	6
Bruising		25.00%	5
Headaches or Dizziness		25.00%	5
Sore mouth/mouth ulcers		20.00%	4
Nausea		15.00%	3
Rapid Heartbeat		15.00%	3
Diarrhea		10.00%	2
Rashes		5.00%	1
Liver Damage		5.00%	1
Neutropenia: Low neutrophil (a type of white blood cell) count		5.00%	1
Fever		0.00%	0
Total Respondents: 20			

MPN specialists are not universally available at every community cancer center, which means some patients and caregivers may need to travel outside their local area to access healthcare services for MF.

Respondents were asked, were you able to receive MF treatment within your home community?

7/20 (35%) answered “no”

Those respondents were then asked, if you could receive MF treatment within your home community, how do you think that would impact your treatment experience?

6/8 (75%) answered that this would have a positive to significant positive impact on their treatment experience

Despite the availability of current treatment options for myelofibrosis (MF), not all patients respond adequately, and even those who do may experience only temporary benefits. Additionally, many patients may not qualify for a potentially curative stem cell transplant. Considering patient responses and

health status, along with patient preference, the range of currently available treatment options may be quite limited.

Respondents were asked to indicate how strongly they agree/disagree with the following statement: “I am/was worried about running out of treatment options to effectively manage my MF”

13/20 (65%) answered that they somewhat to strongly agree

Respondents to this question commented:

- “I am presently on a clinical trial. It appears to help, but if I had to discontinue, I would be quite worried.”
- “Treatment options are very limited, are not curative, have adverse effects and can stop working unexpectedly”
- “No cure. Failed stem cell transplant”
- “I was trying to avoid transplant and hoping for new drugs for treatment”
- “I am now taking Jakafi. This seems like the last option for me.”

Patients and caregivers must carefully weigh many factors when considering a new treatment option, such as how it compares to other options and how it will impact their daily lives.

Respondents were asked to choose the top three factors that are most important to them when considering new MF treatment options:

ANSWER CHOICES	RESPONSES	
Amount/Severity of side effects	94.74%	18
Quality of life during treatment	84.21%	16
The length of time in potential remission	63.16%	12
Financial costs	31.58%	6
Length or frequency of hospital visits/stays	26.32%	5
Outpatient treatment options	21.05%	4
Distance from home	15.79%	3
Number of treatments	10.53%	2
Physician recommendation	10.53%	2

Managing anemia is a significant challenge for patients living with MF. Anemia not only greatly affects patients' daily lives, potentially making extremely burdensome transfusions necessary, but also increases the risk of complications, leading to increased healthcare needs.

Respondents were asked, did you or your loved one have to receive blood/platelet transfusions due to MF?

12/19 (63%) answered yes

Respondents expanded on the impact of required blood transfusions:

- "Frequent hospital visits, which for me are a 45-minute drive each way. I don't like the idea of blood transfusions, although I do appreciate the value"
- Need for blood work (group & cross match) each and every time. Transport to and from hospital. Scheduled transfusion times during the day. Need for pic line.
- "Needing to have transfusions is taxing"
- "The need for transfusions is depressing"

5. Improved Outcomes

Ultimately, patients and caregivers affected by MF strive for an improved quality of life. They recognize that aside from stem cell transplant, which may not be feasible for all patients, current treatment options are not curative. However, reducing symptom burden, enhancing quality of life, and reducing the need for transfusions would significantly benefit these individuals, providing a semblance of normalcy in their lives.

Respondents were asked, ideally, what desired improvements to quality of life would you like to see from new treatments?

- "The doctors very much focus on the treatment and not on how it impacts life afterwards. I would like to see more support for patients who may need assistance navigating through the "new normal." Being able to have treatment closer to home would also be helpful."
- "Feeling normal again"
- "Less fatigue and better controlled anemia"
- "Improved survival"
- "Minimal side effects on quality of life."
- "Lessen need for transfusions"
- "Results long term. Less fatigue and brain fog."

- “Energy and normal platelets”
- “Help fatigue and spleen size/early satiety, and maybe joint issues too, WITHOUT exacerbating anemia and fatigue”
- “Less impact on physiology to the body. Not functioning at a normal level”
- “More energy!”
- “Help with my fatigue, bone pain and anemia”
- “Less visits to the Dr. Smaller spleen size. Not feeling fatigued.”
- “Cure”

Survey respondents were asked, what aspects of this illness do you feel are important to control? The top 3 answers were:

33/57 (58%) - fatigue

31/57 (54%) - anemia/need for transfusions

21/57 (37%) - spleen size

Other responses included:

Bone pain

Progression

Itching/burning

Insomnia

Headaches

Diet/digestion issues

Health care costs

Prolonged life expectancy

Brain fog

Weight loss

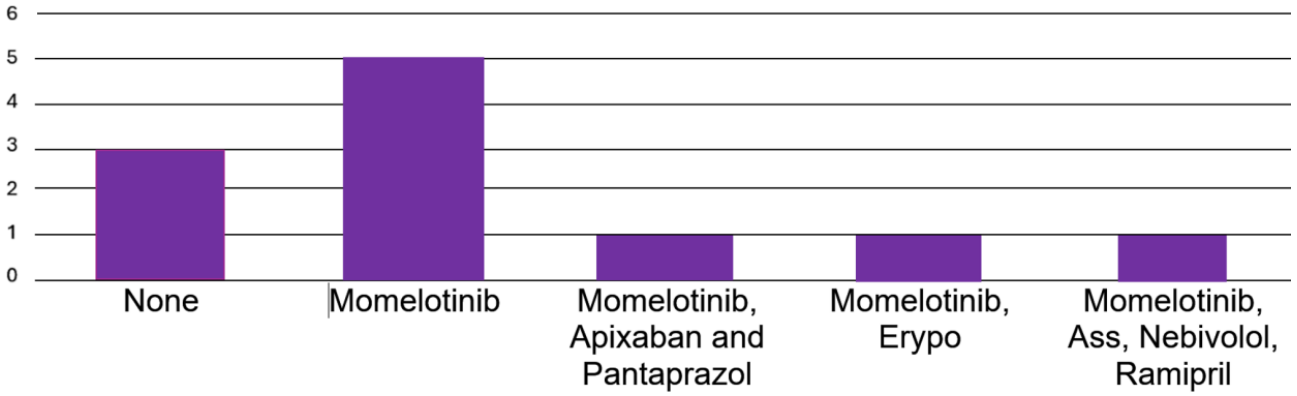
Anxiety

Consideration of the side effects of treatments - e.g. liver damage, bone pain, nausea, etc.

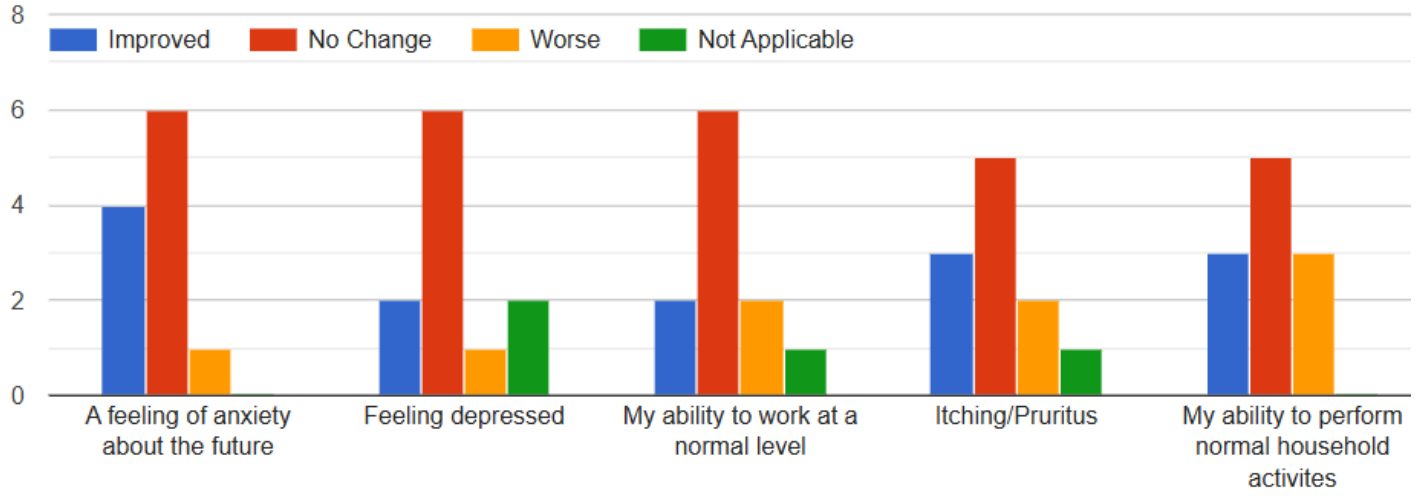
6. Experience With Drug Under Review

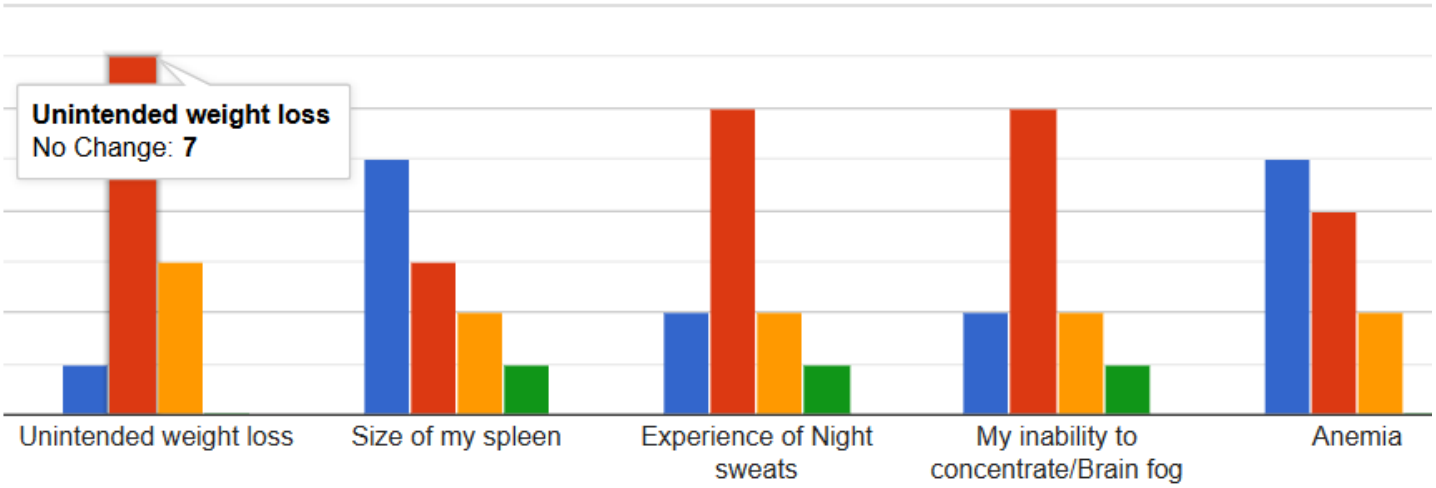
In survey #2, 11 respondents stated that they had been treated with momelotinib to manage their MF. These respondents offered insights based on their personal experiences.

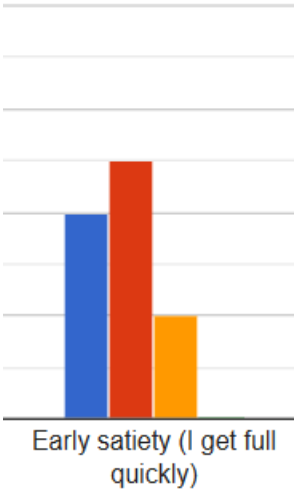
Respondents were asked what treatments they are currently taking. 11 respondents answered this question. Results are reflected in the chart below.



These respondents were then asked how the following aspects of MF were affected after starting treatment with momelotinib. Results are reflected in the charts below.







When using a non-curative treatment, improving quality of life becomes the primary goal for both patients and their caregivers.

The 11 respondents were asked if they feel that momelotinib treatment improved their quality of life. 8/11 (73%) answered yes.

Respondents shared additional thoughts regarding their treatment experience with momelotinib:

“My ferritin levels have improved as have other indications of anemia. Inexplicably though, my platelet counts have risen over 300 pts (570-875) and my MPN doc is a bit mystified. I have been taking the higher dose of 200mg for the last 5 months or so. Due to other co-morbidities I’m not a candidate for a SCT so am hoping it continues to keep me going in the right direction”

“My blood counts and spleen size have remained essentially the same as they were before I started momelotinib, which I take as a good outcome. I generally feel fine, though I still experience fatigue, but it's not debilitating. I have had some issues with bloating and gas, but my doctor prescribed famotidine (Pepcid) which has helped considerably, and the side effects have now largely resolved”

“No side effects”

“It was a life saver. I became transfusion independent for 6 years. When it stopped working, I had a bone marrow transplant. Great drug.”

“Definitely not needing bloodwork every single week with the Jakafi making my anemia tank and no more transfusions on OJJAARA is a gift! I am still anemic. I would say I am 70% of where I should be for my red blood cells, I feel like I’m fully functional, where I was at diagnosis. But on Jakafi I was at 48% of where I needed to be. And it was a fog. I was told the purpose for going on either of these medications was to reduce my splenomegaly so I could have an SCT, the only cure for MF. OJJAARA Reduced my spleen 17% after 3 months of a 100mg dose. They increased my dose to 200 mg and I’m hoping now that I’ve been on that for 4 more months that my spleen is reduced 35%. It was 26cm at diagnosis in July 2023.”

One patient interviewee who is currently using momelotinib (since January 2024) as his fourth treatment for MF shared the many benefits that he has seen so far thanks to momelotinib:

“This is the **best drug I’ve taken for this disease so far**. I’m better than I’ve been for a long time.”

“**I can walk** and do all kinds of cool things I couldn’t do for a long, long time”. At first, he started to walk with a walker and now he can walk using just a cane.

He was having to go for transfusions weekly and his **last transfusion came after 3 weeks of not needing one.**

He shared that momelotinib has **increased his ability to start doing some things around the house and has made a difference in how much his caregiver, his wife, has to do**. “It's made a difference in how much she has to do. I still don't do an awful lot around here, but I do some stuff now. I do still sleep a lot. Two or three times a day. 3:00 is nap time every day.”

“Another thing is my **memory**. I used to get brain fog all the time and I don't get that so much anymore with the momelotinib. I did with the rest. Of all the drugs I’ve taken this is the best one so far.”

When asked how long it took before he noticed a difference in his symptoms, he stated:

“Pretty much right from when I first started it. In fact, that's why I get a little antsy when I don't have any medication left or I don't have a lot left. If I don't have more than a week left then I start getting antsy 'cause I don't really want to have to go back to Jakavi, I'd rather stay on this because as I say, it has been as far as we're both concerned, the best one so far.”

He explained that he is currently receiving momelotinib treatment through a compassionate access program and he is afraid because he has been seeing great results and he doesn’t know how long he might be able to keep getting the medication.

He is hoping that momelotinib is quickly reimbursed for Canadians so that he doesn’t have to be concerned about losing access to this treatment.

7. Companion Diagnostic Test

8. Anything Else?

There are currently no approved treatments specifically for anemia associated with MF. Patients rely on burdensome long-term blood transfusions or on drugs that stimulate erythropoietin production. However, these may not provide long-term symptom relief or target the root causes of their disease. This need that remains unmet with current treatment options is critical for patients who don’t respond well to these options or who develop anemia while on JAK inhibitors.

Currently available JAK inhibitors do help with some MF symptoms including splenomegaly, but often do not improve anemia and can even worsen it as a side effect.

Momelotinib is specifically developed to address the unmet need of managing anemia and other symptoms such as splenomegaly in patients with MF. It provides an additional treatment option for this patient population, offering decreased dependency on transfusions, and enhancing overall well-being and improved outcomes for patients.

73% of respondents who have experienced treatment with momelotinib stated that they feel that momelotinib treatment improved their quality of life. This is significant.

Our patient organizations would strongly advise the CDA to recommend reimbursement of momelotinib for the treatment of disease-related splenomegaly or symptoms, and anemia in adult patients with primary myelofibrosis, post polycythemia vera myelofibrosis or post essential thrombocythemia myelofibrosis who are Janus Kinase (JAK) inhibitor naive or have been treated with a JAK inhibitor.

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.

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

No

1. 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

2. 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 - LLSC

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
GSK		X		
Novartis				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, LLSC
Patient Group: The Leukemia & Lymphoma Society of Canada (LLSC)
Date: June 27, 2024

Table 2: Financial Disclosures - CMPNN

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	
Protagonist Therapeutics			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: John Clark

Position: Advocacy Committee Lead
Patient Group: Canadian MPN Network
Date: 26 June 2024

Clinician Group Input

CADTH Project Number: PC0355

Generic Drug Name (Brand Name): momelotinib

Indication: For the treatment of disease-related splenomegaly or symptoms, and anemia in adult patients with primary myelofibrosis, post polycythemia vera myelofibrosis or post essential thrombocythemia myelofibrosis who are Janus Kinase (JAK) inhibitor naïve or have been treated with a JAK inhibitor.

Name of Clinician Group: OH (CCO) Hematology Cancer disease site Drug Advisory Committee

Author of Submission: Dr. Tom Kouroukis

1. About Your Clinician Group

Please describe the purpose of your organization. Include a link to your website (if applicable).

<Enter Response Here>

2. Information Gathering

Information was gathered by videoconferencing.

3. Current Treatments and Treatment Goals

Current treatments include ruxolitinib and fedratinib as well as supportive care therapies including transfusions and erythropoietin. Some selected patients will also proceed to allogeneic transplant.

Current treatments are designed to reduce symptoms, improve blood counts or splenomegaly, and reduce transfusion requirements.

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.

Some treatments are not well tolerated and not very effective.

Momelotinib may be preferred over ruxolitinib and fedratinib due to decreased cytopenias as seen in the trials.

5. Place in Therapy

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

This is a treatment option available to the existing therapies.

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?

Patients with significant anemia may benefit with momelotinib in comparison to other available therapies.

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?

Symptom burden, blood counts and splenomegaly. Patients would be assessed monthly or as needed.

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

Significant intolerance, and clear, worsening or lack of response.

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 settings with specialists who have experience in managing myelofibrosis.

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.

3. 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) provided a secretariat function to the group.

4. 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.

5. 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: Dr. Tom Kouroukis

Position: Lead, OH (CCO) Hematology Cancer DAC

Date: 20-06-2024

☒ **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. Selay Lam

Position: Member, OH (CCO) Hematology Cancer DAC

Date**:** 20-06-2024

☒ 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: Dr. Lee Mozessohn

Position: Member, OH (CCO) Hematology Cancer DAC

Date**:** 20-06-2024

☒ 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

	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 4

Name: Dr. Jordan Herst

Position: Member, OH (CCO) Hematology Cancer DAC

Date**:** 20-06-2024

☒ 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

	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 5

Name: Dr. Christopher Cipkar

Position: Member, OH (CCO) Hematology Cancer DAC

Date**:** 20-06-2024

☒ 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

	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.

X in the appropriate dollar range cells for each company.

Declaration for Clinician 6

Name: Dr. Guillaume Richard-Carpentier

Position: Member, OH (CCO) Hematology Cancer DAC

Date**:** 27-06-2024

☒ 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.

X in the appropriate dollar range cells for each company.

CADTH Project Number: PC0355-000

Indication: Momelotinib is indicated for the treatment of disease-related splenomegaly or symptoms, and anemia in adult patients with primary myelofibrosis, post polycythemia vera myelofibrosis or post essential thrombocythemia myelofibrosis who are Janus Kinase (JAK) inhibitor naïve or have been treated with a JAK inhibitor.

Name of Clinician Group: LLSC Clinician Network & Canadian MPN Clinician Group

Author of Submission: Colleen McMillan, LLSC

1. About Your Clinician Group

The LLSC Clinician Network is a group of Canadian clinicians with experience with myelofibrosis.

The Canadian MPN group is a dedicated collaborative group of physicians across Canada. Our mission is to enhance the care of patients with MPNs through harmonization of practice, facilitate cutting-edge research, and foster national collaboration. Our group is experienced in treating all MPNs including myelofibrosis.

2. Information Gathering

The Leukemia Lymphoma Society of Canada (LLSC) and Dr. Shireen Sirhan facilitated information gathering through a series of interviews and discussions with clinicians from various Canadian cancer centres, who have experience with myelofibrosis.

3. Current Treatments, Treatment Goals and Unmet Need

- Myelofibrosis is a complex and debilitating malignancy characterized by the excessive accumulation of fibrous tissue in the bone marrow, leading to anemia, splenomegaly, and debilitating constitutional symptoms. While effective treatment options have emerged over the years, the management of anemia remains a critical challenge in myelofibrosis care. Anemia not only significantly impacts patients' quality of life but also contributes to increased morbidity and mortality and healthcare resource utilization. Particularly concerning is the observation that currently available JAK inhibitors, which can be effective in addressing some symptoms and splenomegaly, fail to improve anemia and exacerbate anemia as an on-target side effect. For example, ruxolitinib is a JAK inhibitor that is used as standard of care and carries anemia as a frequent side effect, limiting tolerability and clinical use at therapeutic doses.

- There are no approved treatments for myelofibrosis-associated anemia.

- Anemia, as well as the need for life-saving transfusions, significantly impact patient quality of life.

- Erythropoietin stimulating agents are currently used off-label to treat myelofibrosis associated anemia. However, many patients do not respond to erythropoietin and other patients have only a limited duration of response. Patients experience insufficient relief from symptoms.

- In our clinical experience, patients express mixed results with transfusions. For some, transfusions do not change patient quality of life or their ability to function. Even for those who report improvement with transfusions, the results are transient. Patients start to feel worse as their hemoglobin levels decrease over time. Treatments that are able to decrease the need for transfusions, which are both logistically intensive and carry risks to patients, are highly desired in this population.

- For high-risk patients who are eligible for allogenic stem cell transplant, fewer transfusions may lead to better outcomes. Higher transfusion burdens carry risks of iron overload and alloimmunization, which can adversely impact engraftment and post-transplant outcomes.

- For patients who are not transplant eligible, or have low-risk myelofibrosis, the focus is on improving quality of life. The requirement to attend frequent hospital appointments for red blood cell transfusion can have a significant adverse effect on quality of life for patients.

- Thus, the prospect of momelotinib, a novel therapeutic agent targeting anemia in addition to splenomegaly and symptoms in myelofibrosis, holds great promise in meeting the unmet needs of myelofibrosis patients.

- Momelotinib gives the potential for patients to achieve an overall sense of better well-being, and improvement in functions, while mitigating risks of anemia that may otherwise preclude the effective use of other JAK inhibitors. For example, myelofibrosis patients can often feel too exhausted, or too unwell to be active, get up or participate in daily life activities. Momelotinib can give them the chance to do usual life activities such as to going out and spending time, like going on walks with their family, feeling more, “normal” and as a result achieve a better quality of life.

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.

See above.

5. Place in Therapy

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

I

- Limited Treatment Options: Currently there are limited treatment options. Anemia significantly compromises patients' quality of life and is associated with increased rates of hospitalization and mortality. Existing treatments for anemia in myelofibrosis, such as erythropoietin stimulation agents and blood transfusions are often inadequate due to transient/limited response and risks, leaving a critical gap in therapeutic options.

- Potential Clinical Benefits: Clinical data for momelotinib demonstrates its potential to effectively address anemia and myelofibrosis symptoms and splenomegaly, potentially leading to improved hemoglobin levels, reduced transfusion dependency, and enhanced overall well-being for patients.

- Innovative Mechanism of Action: Uniquely, momelotinib also inhibits the activin receptor type 1 (ACVR1) enzyme which is implicated in ineffective erythropoiesis.

- This dual inhibition of JAK1/2 and ACVR1 contributes to momelotinib's ability to alleviate anemia symptoms, reduce spleen size, and improve constitutional symptoms in patients with myelofibrosis. This ability to address anemia is a key differentiator for momelotinib compared to other JAK inhibitors, which often cause or exacerbate pre-existing cytopenias – notably, anemia.

- Clinicians recommend having this treatment available for JAK inhibitor naïve and JAK inhibitor experienced patients.

- This new treatment has not yet demonstrated a reduction in the risk of transformation to acute leukemia or mitigate the need for curative allogeneic stem cell transplantation in eligible patients. However, reducing symptom burden, splenomegaly, and addressing the burden of anemia means that momelotinib would provide a new avenue for physicians to better manage myelofibrosis patients with anemia, thereby alleviating their suffering and improving clinical outcomes – both in transplant-eligible and ineligible groups. Clinicians remind CDA that for those who are transplant-eligible, higher transfusion burdens carry risks of iron overload and alloimmunization, which can adversely impact engraftment and post-transplant outcomes.

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?

- Momelotinib does have a clear unique advantage over currently available treatments in addressing the unmet need of myelofibrosis associated anemia.

- Myelofibrosis patients who are at risk of anemia, or are already anemic, would benefit from momelotinib over the current standard of care option – i.e., ruxolitinib. Patients who are borderline from a transfusion dependency perspective and are started on ruxolitinib, can often become transfusion dependent because it can lower blood counts, prominently hemoglobin, resulting in a myriad of transfusion-associated risks.

- Some clinicians in this submission experienced the use of momelotinib through clinical trials. They noted that some of their transfusion dependent patients, who were randomized to momelotinib were able to become transfusion independent.

- Clinicians feel that anemia is an essential point for CDA to note as the reimbursement criteria is considered. Clinicians believe that anemia as a criterion, not just transfusion dependence, is critical to addressing the unmet need and helping patients at risk of transfusion dependence avoid this problematic issue.

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?

- Momelotinib is a JAK1/JAK2 inhibitor and belongs to a class of treatment that clinicians are familiar with using and managing side effects
- Treatment response would be:
    - Stable disease or
    - Improvement in symptom burden, decrease in spleen volume, improvement in hemoglobin and/or reduction in transfusions

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

Clinicians believe that at least 6 months is required for assessment of efficacy. Factors to consider for lack of efficacy include:

- Increase in transfusion requirement accompanied by:
- Increase in symptom burden
- Increase in spleen volume
- Severe therapy-related thrombocytopenia or neutropenia

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]?

- Momelotinib is an oral medication that patients take daily at home
- A hematologist/oncologist would be required to oversee the patient's diagnosis and treatment with momelotinib

6. Additional Information

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.

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

No

7. 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

8. 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: Dr. Shireen Sirhan

Position: Assistant professor Mcgill University -Jewish General Hospital

President Canadian MPN group

Date: 26-06-2024

☒ 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			X	
GSK		X		
Janssen		X		
DISC Medicine		X		
Medison Pharma	X			

SOBI Pharma	X			

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

Declaration for Clinician 2

Name: Jaroslav F. Prchal

Position: Associate Professor, McGill University

Date: 26-06-2024

☒ 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**
No conflict of interest				

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

Declaration for Clinician 3

Name: Sonia Cerquozzi

Position: Clinical Assistant Professor

Date: 26-06-2024

☒ 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

	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			
BMS	X			
Incyte	X			
Medison Pharma Canada	X			
Takeda	X			
Medlior Health	X			
Pfizer	X			
Abbvie	X			

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

Declaration for Clinician 4

Name: Dawn Maze

Position: Hematologist, Princess Margaret Cancer Centre

Date: 26-06-2024

☒ 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
Novartis		X		
GSK		X		

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

Declaration for Clinician 5

Name: Lynda Foltz

Position: Hematologist

Date: 26-06-2024

☒ 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

	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		
Medison Pharma	x			

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

Declaration for Clinician 6

Name: Shreyash Dalmia

Position: Clinical Fellow, Malignant Hematology & Hematologist

Date: 06/06/2024

Y **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 6: 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**
Add company name				

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

Declaration for Clinician 7

Name: Chris Hillis

Position: Hematologist

Date: 26-06-2024

X **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 7: 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**
AstraZeneca		X		
Pfizer		X		
Janssen		X		
Paladin	X			
Bristol-Meyers Squibb	X			
Novartis	X			
GSK	X			
DISC Medicine	X			
Medison Pharma	X			
SOBI Pharma	X			

Declaration for Clinician 8

Name: Stephanie Lee

Position: Hematologist, Assistant Professor at the University of Toronto

Date: 26-06-2024

☒ **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 8: Conflict of Interest Declaration for Clinician 8

Company	**Check appropriate dollar range***

	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Medison		X		
Novartis	X			

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

Declaration for Clinician 9

Name: Dr. Brian Leber

Position: Professor of Medicine (Hematology) , McMaster University; Disease Site Group Head- Leukemia, Juravinski Cancer Centre/Hamilton Health Sciences

Date: 26-06-2024

☒ 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 9: 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		
SOBI Pharma		X		

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