

CADTH Reimbursement Recommendation

Fedratinib (Inrebic)

Indication: Treatment of splenomegaly and/or disease-related symptoms in adult patients with intermediate-2 or high-risk primary myelofibrosis, post-polycythemia vera myelofibrosis, or post-essential thrombocythemia myelofibrosis, including patients who have been previously exposed to ruxolitinib

Sponsor: Celgene Inc., a Bristol Myers Squibb Company

Final Recommendation: Reimburse with conditions

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Funding: CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

Summary

What is the CADTH reimbursement recommendation for Inrebic?

CADTH recommends that Inrebic be reimbursed by public drug plans for the treatment of splenomegaly and/or disease-related symptoms in adults with myelofibrosis if certain conditions are met.

What are the conditions for reimbursement?

Inrebic should only be reimbursed if it is prescribed by a clinician with expertise in treating and managing myelofibrosis and if it does not cost more than other Janus kinase (JAK) inhibitors.

Which patients are eligible for coverage?

Inrebic should only be provided to patients with myelofibrosis who cannot take or tolerate Jakavi. Inrebic should not be prescribed to patients who progress on Jakavi or are taking other treatments for splenomegaly and/or myelofibrosis-related symptoms.

Why did CADTH make this recommendation?

Evidence from a clinical trial demonstrated that Inrebic reduces spleen size and relieves myelofibrosis-related symptoms better than placebo. Inrebic is more expensive than Jakavi, but there is no evidence that it is more effective.

Key Messages

- Clinical evidence suggests that the JAK inhibitor Inrebic should be reimbursed as a treatment option for adults with myelofibrosis who cannot take or tolerate Jakavi. Inrebic cannot be prescribed to those who progress on Jakavi.
- There is insufficient evidence to justify a cost premium for Inrebic over other JAK inhibitors reimbursed for the treatment of myelofibrosis.
- If Inrebic is not reimbursed by public payers, best available therapy will be the only other treatment option for patients who cannot take Jakavi.

What is myelofibrosis?

Myelofibrosis is a rare form of blood cancer. There are approximately 1,800 people with myelofibrosis in Canada. People with myelofibrosis have a shortened life expectancy and may have an enlarged spleen. Common symptoms include pain, fullness, feeling tired, excessive night sweats, and fever.

What is Inrebic?

Inrebic (fedratinib) is a JAK inhibitor. It is approved by Health Canada for the treatment of enlarged spleen and/or disease-related symptoms in adult patients with myelofibrosis, including patients who have been previously treated with Jakavi. Inrebic is a pill that can be taken by mouth once a day.

How much does Inrebic cost?

Treatment with Inrebic is expected to cost approximately \$338 per day per patient.

What other treatments are available for myelofibrosis?

Most patients are currently treated with Jakavi, which is used as a first-line treatment for myelofibrosis. Prior to the approval of Inrebic, Jakavi was the only JAK inhibitor available to treat myelofibrosis. Cytoreductive treatments such as hydroxyurea and interferon therapies are the only treatment options for patients who cannot take Jakavi.

Unmet needs in myelofibrosis

Jakavi cannot be used in all patients with myelofibrosis, and some patients treated with Jakavi will not be able to tolerate the side effects. Another first-line treatment option would be useful for these patients.

How much do other treatments cost?

Jakavi costs \$173 per day per patient.

Recommendation

The CADTH pCODR Expert Review Committee (pERC) recommends that fedratinib be reimbursed for the treatment of splenomegaly and/or disease-related symptoms in adult patients with intermediate-2 or high-risk primary myelofibrosis, post-polycythemia vera myelofibrosis, or post-essential thrombocythemia myelofibrosis only if the conditions listed in Table 1 are met.

Rationale for the Recommendation

In 1 double-blind, randomized, placebo-controlled, phase III trial (JAKARTA, N = 289) in patients with myelofibrosis who had not received previous treatment with a JAK inhibitor, a significantly greater proportion of patients treated with 400 mg fedratinib (36.5%) achieved spleen response ($\geq 35\%$ reduction in spleen volume 24 weeks after treatment initiation and confirmed 4 weeks later) compared with those treated with placebo (1%). This difference was statistically significant in favour of fedratinib (mean difference 35.4%; 97.5% confidence interval [CI], 24.2 to 46.7; $P < 0.0001$). In addition, treatment with fedratinib was associated with greater relief in disease-related symptoms, as measured by the Total Symptom Score (TSS) on the modified Myelofibrosis Symptom Assessment Form (MFSAF). Specifically, a statistically significant and clinically meaningful difference was observed at the end of cycle 6, where the proportion of patients who had a 50% or greater reduction in the TSS from baseline was 39.6% in the fedratinib treatment group and 8.2% in the placebo treatment (mean difference = 31.3%; 95% CI, 18.0 to 44.6; $P < 0.0001$). The effects of fedratinib on other outcomes that were identified by patients as important, such as survival and health-related quality of life (HRQoL), were inconclusive based on results of the JAKARTA study. However, fedratinib does meet the needs identified by patients: an additional oral treatment for myelofibrosis and decreased burden of symptoms.

Results from an indirect treatment comparison (ITC) suggested that a greater proportion of JAK inhibitor-naïve patients treated with fedratinib had a reduction in spleen volume of 35% or more 24 weeks after treatment initiation compared with those treated with ruxolitinib (between-group difference = 12.3%; 95% CI, 0.6 to 24.0). There was no difference in the relative efficacy of fedratinib versus ruxolitinib in achieving a 50% or greater reduction in TSS (between-group difference = -9.4%; 95% CI, -23.9 to 5.2).

The sponsor's submitted price of fedratinib is \$84.39 per 100 mg capsule, with an annual treatment cost of \$123,213. CADTH reanalyses of the sponsor's economic model demonstrated the incremental cost-effectiveness ratio (ICER) for fedratinib is \$88,698 per quality-adjusted life-year (QALY) compared with best available therapy (BAT) in JAK inhibitor-naïve patients who are assumed to not have received subsequent treatment with ruxolitinib.

Table 1: Reimbursement Conditions and Reasons

Reimbursement condition	Reason
Initiation	
1. Fedratinib should be initiated in patients for whom ruxolitinib is contraindicated or patients who are intolerant of ruxolitinib.	In the JAKARTA study, compared with placebo, patients who were treated with fedratinib 400 mg once daily showed benefits in spleen volume reduction and myelofibrosis-related symptom relief from baseline to the end of cycle 6. However, based on indirect evidence, treatment with fedratinib does not appear to offer any efficacy benefit over ruxolitinib in symptom relief, and the benefit in spleen volume reduction was small in the JAK inhibitor–naive patient population when compared to ruxolitinib. Ruxolitinib is currently the standard first-line treatment for patients with myelofibrosis, and clinicians have experience using this drug and are comfortable with its safety profile. In the absence of robust evidence demonstrating a benefit of fedratinib over ruxolitinib, ruxolitinib should be the first-line treatment of choice unless there is a contraindication.
2. Fedratinib should not be reimbursed in patients who experience disease progression following treatment with ruxolitinib.	There is no robust evidence demonstrating a benefit of fedratinib as a second-line treatment in patients who have progressed following ruxolitinib treatment.
3. Patient must have good performance status.	In the JAKARTA study, patients were required to have an ECOG performance status of 0 to 2.
Renewal	
1. Patients should be assessed for a response to treatment with fedratinib every 3 to 6 months.	Renewal criteria should be similar to the criteria used by public drug plans for other JAK inhibitors reimbursed for the treatment of myelofibrosis.
2. A response to treatment with fedratinib is defined as either of the following based on clinical assessment: <ul style="list-style-type: none"> • evidence of reduction in spleen size • symptom improvement. 	The response to treatment should be defined in a manner similar to the criteria used by each of the public drug plans for reimbursement of other JAK inhibitors for the treatment of myelofibrosis.
Discontinuation	
1. Treatment with fedratinib should be discontinued in patients who demonstrate any 1 of the following: <ul style="list-style-type: none"> • progressive increase in spleen size • return of constitutional symptoms • development of serious adverse events. 	In the JAKARTA study, treatment with fedratinib was discontinued for any of the following reasons: disease progression, unacceptable toxicity, or relapse.
Prescribing	
1. The patient should be under the care of a clinician with expertise in treating and managing myelofibrosis.	Accurate diagnosis by a clinician with experience and expertise in treating and managing myelofibrosis is important to ensure that fedratinib is prescribed only for appropriate patients.
2. Fedratinib should not be prescribed in combination with other JAK inhibitors or other therapies.	There is no evidence to determine the effects of fedratinib when used in combination with other JAK inhibitors or other therapies.

Reimbursement condition	Reason
Pricing	
<p>1. The drug plan cost of fedratinib should not exceed the drug plan cost of treatment with the least costly JAK inhibitor reimbursed for the treatment of splenomegaly and/or disease-related symptoms.</p>	<p>At the submitted price, fedratinib (\$337.57 per day) is more costly than ruxolitinib (\$173.26 per day). Given the lack of direct comparative evidence to compare these 2 treatments, and the uncertainty associated with an indirect comparison of JAK inhibitors used to treat myelofibrosis, there is insufficient evidence to justify a cost premium for fedratinib over the least expensive JAK inhibitor reimbursed for the treatment of splenomegaly and/or disease-related symptoms in adults with intermediate-2 or high-risk primary myelofibrosis, post-polycythemia vera myelofibrosis, or post-essential thrombocythemia myelofibrosis.</p>

ECOG = Eastern Cooperative Oncology Group; JAK = Janus kinase.

Implementation Guidance

1. The product monograph for fedratinib includes a warning that thiamine levels must be assessed in all patients before initiating treatment and periodically throughout treatment. Availability and reimbursement of thiamine testing may vary across jurisdictions.
2. In the JAKARTA study, patients were required to have an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 2. The clinical experts consulted by CADTH indicated that the clinicians would like to offer fedratinib treatment to patients with poorer performance status due to underlying myelofibrosis.
3. In assessing the response to treatment (see Renewal Condition 2), the magnitude of the reduction in spleen size and the degree of symptom improvement should be defined by individual public drug plans in line with the reimbursement criteria established for other myelofibrosis treatments. In most cases, clinical assessment is sufficient for detecting a change in spleen size to determine whether a patient is responding to treatment with fedratinib. However, diagnostic imaging may be required if the spleen is not palpable.

Discussion Points

- pERC was unable to conclude whether treatment with fedratinib offers any survival benefit in patients with myelofibrosis, which was identified as important by patients and clinicians. Although overall survival and progression-free survival were planned secondary end points in the JAKARTA study, they could not be evaluated due to early termination of the study. Therefore, the effect of fedratinib treatment on these outcomes is unknown.
- HRQoL was identified as an outcome important to patients and was assessed as an exploratory outcome in the JAKARTA study using the EuroQol 5-Dimensions (EQ-5D) questionnaire. However, given that a formal statistical comparison was not performed for any HRQoL outcomes, pERC was unable to conclude whether treatment with fedratinib offers any HRQoL benefit in patients with myelofibrosis.
- pERC considered that fedratinib should be used with caution in patients at risk for serious and fatal encephalopathy (including Wernicke encephalopathy) and thiamine deficiency. Clinicians need to exercise caution in those patients at increased risk of fedratinib toxicity.

- There is no robust evidence demonstrating a benefit of fedratinib as a second-line treatment in patients who have progressed following ruxolitinib treatment. One ITC in JAK inhibitor–experienced patients suggested that treatment with fedratinib may be associated with a higher spleen response rate and higher symptom response rate compared with BAT. However, these results are associated with a substantial risk of bias. pERC also acknowledged that 1 phase II, single-arm, open-label study (JAKARTA 2) involving ruxolitinib-experienced patients with intermediate- to high-risk myelofibrosis supported the beneficial effect of fedratinib on reduction in spleen volume and symptom relief, but there was substantial uncertainty associated with the results of this study due to the open-label administration of fedratinib, small sample size, lack of comparator group, and short study duration.

Background

Fedratinib has a Health Canada indication for the treatment of splenomegaly and/or disease-related symptoms in adult patients with intermediate-2 or high-risk primary myelofibrosis, post-polycythemia vera myelofibrosis, or post-essential thrombocythemia myelofibrosis, including patients who have been previously exposed to ruxolitinib. Fedratinib is a selective JAK2 inhibitor. It is available as 100 mg capsules, and the Health Canada–approved dose is 400 mg taken orally once daily for patients with a baseline platelet count of $50 \times 10^9/L$ or greater.

Summary of Evidence

To make their recommendation, the Committee considered the following information:

- A systematic review including 1 randomized controlled trial in adult patients with myelofibrosis
- Patients’ perspectives gathered by 3 patient groups, including the Leukemia and Lymphoma Society of Canada (LLSC), the Canadian Myeloproliferative Neoplasms (MPN) Research Foundation, and the Canadian MPN Network
- Input from 2 clinical specialists with expertise diagnosing and treating patients with myelofibrosis
- Input from 1 clinician group, including 4 hematologists and a pharmacist, on behalf of the Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee
- Input from the participating drug plans
- A review of the pharmacoeconomic model and report submitted by the sponsor

Summary of Patient Input

Three patient groups provided input for this submission: the LLSC, the Canadian MPN Research Foundation, and the Canadian MPN Network. Patient perspectives were obtained from surveys, discussions with patients and caregivers, and phone or in-person interviews. Four patients and 4 caregivers in these groups had experience with fedratinib in the second-line setting after ruxolitinib through participation in a clinical trial.

The following is a summary of key input from the perspective of the patient groups:

- Patients with myelofibrosis experience fatigue, loss of appetite, bone pain, pain and discomfort related to their enlarged spleen, fever and night sweats, shortness of breath, bruising, and bleeding. In addition, patients experienced impaired cognition and concentration as well as psychological effects, such as anxiety and difficulty sleeping. These cancer symptoms negatively impact the patient's quality of life.
- Patients expressed that there are limited treatment options for patients diagnosed with myelofibrosis and that currently available treatments include ruxolitinib and best supportive care. When these therapies become ineffective, patients become dependent on blood transfusions. Patients want treatments that will cure their disease and improve their quality of life. Cost and accessibility are also factors that need to be considered.
- The patient groups believe that fedratinib will provide an additional treatment option to patients with myelofibrosis that has the potential to improve their HRQoL. In addition, fedratinib will provide hope to patients that have been diagnosed with an incurable disease. The patient groups believe that fedratinib will have a positive impact on patients, their caregivers, and the health care system.

Clinical Trials

The systematic review included 1 double-blind, randomized, placebo-controlled, phase III trial of patients with primary or secondary myelofibrosis (post-polycythemia vera myelofibrosis or post-essential thrombocythemia myelofibrosis; JAKARTA, N = 289) who did not receive prior treatment with a JAK2 inhibitor. Eligible patients were randomized to receive fedratinib 400 mg (n = 96), fedratinib 500 mg (n = 97), or placebo (n = 96) once daily for 6 consecutive 28-day treatment cycles. During the treatment period, patients continued to receive their assigned treatment until disease progression or occurrence of intolerable adverse events related to the treatment. Given that the 500 mg dose of fedratinib is not approved in Canada, the fedratinib 400 mg dose was the focus of the CADTH review. The JAKARTA study was terminated early due to the risk of encephalopathy associated with fedratinib therapy. At the time of study termination, all patients had either completed the first 6 cycles or had previously permanently discontinued treatment. There were ■ patients in the fedratinib 400 mg arm (■%) and ■ patients in the placebo arm (■%) who completed 6 cycles of treatment.

The major limitations of the JAKARTA study include the potential biases on the study results due to the imbalanced patients' baseline characteristics and underpowered subgroup analyses. In addition, the discontinuation rates were high across the treatment groups. Discontinuations in the fedratinib arm were mostly due to adverse events, whereas the primary reason of treatment discontinuation in the placebo group was lack of efficacy. The potential impact of substantial and disproportional missing data may bias some of the efficacy outcome measurements. In addition, due to the early termination of the JAKARTA study, overall survival and progression-free survival could not be assessed.

Outcomes

Outcomes were defined a priori in CADTH's systematic review protocol.

The Committee discussed the following: spleen response, disease-related symptom relief, and HRQoL.

The primary outcome in the JAKARTA study was spleen response rate at the end of cycle 6, defined as the proportion of patients with 35% or greater reduction in spleen volume at week 24 and confirmed 4 weeks later. Change in spleen volume was measured by MRI or CT scan. A minimal important difference for spleen response was not identified.

Change in myelofibrosis-related symptoms was evaluated using TSS in the modified MFSAF. The modified MFSAF is a myelofibrosis-specific, patient-reported measure of HRQoL. Six myelofibrosis symptoms (night sweats, pruritus, abdominal discomfort, early satiety, pain under ribs on left side, and bone or muscle pain) are rated at their worst moment during the previous 24 hours. Each symptom is measured on a scale from zero (absent) to 10 (worst imaginable). The TSS is the sum of the scores for each symptom. The proportion of patients with a 50% or greater reduction from baseline to week 24 in the TSS of the modified MFSAF was a secondary efficacy outcome in the JAKARTA study.

HRQoL was measured using the EQ-5D, a generic HRQoL instrument that has been applied to a wide range of health conditions and treatments. However, EQ-5D has not been validated in patients with myelofibrosis specifically. HRQoL was an exploratory outcome in the JAKARTA study.

Overall survival and progression-free survival were identified as relevant outcomes in the CADTH review protocol and were planned secondary end points in the JAKARTA study; however, they could not be evaluated due to early termination of the JAKARTA study.

Efficacy

Spleen Response

A greater proportion of patients in the fedratinib 400 mg group (36.5%) achieved spleen response compared with the placebo group (1%), which was a statistically significant difference in favour of fedratinib 400 mg (between-group difference = 35.4%; 97.5% CI, 24.2 to 46.7; $P < 0.0001$). Similar results were observed for other outcomes measuring spleen response, such as a 25% or greater reduction in spleen volume at week 24 and confirmed 4 weeks later and percentage of change in spleen volume from baseline to week 24. According to the clinical experts consulted by CADTH, the benefit gained in spleen response are clinically meaningful.

Disease-Related Symptom Relief

Treatment with fedratinib was associated with greater relief in disease-related symptoms, as measured by the TSS. At the end of cycle 6, the proportion of patients who had a 50% or greater reduction in the TSS from baseline was significantly greater in the fedratinib 400 mg arm (39.6%) than in the placebo arm (8.2%; mean difference = 31.3%, 95% CI, 18.0 to 44.6; $P < 0.0001$). The clinical experts agreed that the between-group differences are clinically meaningful.

HRQoL

HRQoL was an exploratory end point in the JAKARTA study. Only descriptive summary statistics were provided for the EQ-5D utility index scores and the visual analogue scale (VAS) scores. The mean change in EQ-5D utility index scores from baseline to the end of cycle 6 was 0.05 (95% CI, 0 to 0.09) in the fedratinib 400 mg group and -0.05 (95% CI, -0.11 to 0.01) in the placebo group. The mean change in EQ-5D VAS scores in the fedratinib group was 6.2 (95% CI, 1.8 to 10.5) at the end of cycle 6, and -0.9 (95% CI, -7.7 to 5.8) in the placebo group.

Harms (Safety)

Most patients reported adverse events (AEs) during the 6-cycle treatment period in the JAKARTA study: █% in the fedratinib 400 mg group and █% in the placebo group. The most common AEs reported in both groups were gastrointestinal disorders: █% in fedratinib group and █% in placebo group. The incidence of serious AEs was similar between the fedratinib 400 mg and placebo groups (█% and █%, respectively). More patients in the fedratinib group withdrew from treatment due to AEs (█% in fedratinib group versus █% in placebo group). More deaths occurred in the placebo group than in the fedratinib group (█% versus █%, respectively). In the fedratinib group, the primary cause of death was AE in █ and progressive disease in █. In the placebo group, the primary cause of death was AE in █ and progressive disease in █.

In terms of notable harms, █ treated with fedratinib 400 mg (█%) reported █ compared with placebo (█%) up to cycle 6. The incidence of █ was █. Fedratinib (█%) was also found to be related to █ compared with placebo (█%).

Indirect Evidence

Two ITCs submitted by the sponsor were summarized and critically appraised. In both ITCs, fedratinib was compared with BAT for JAK inhibitor–experienced patients with myelofibrosis or to ruxolitinib for JAK inhibitor–naïve patients with myelofibrosis. The ITCs included a systematic literature review followed by a matching-adjusted indirect comparison and a simulated treatment comparison (JAK inhibitor–experienced comparison only). Spleen volume reduction and TSS reduction at week 24 were the efficacy outcomes included in the ITCs.

In the ITC for JAK inhibitor–experienced patients, the results suggested that treatment with fedratinib 400 mg once daily was associated with greater proportion of patients achieving a 35% or greater reduction in spleen volume at week 24 compared with BAT (between-group difference = 12.5%; 95% CI, 4.5 to 20.9). Treatment with fedratinib was also associated with a greater proportion of patients achieving a 50% or greater reduction in TSS from baseline to week 24 compared to BAT (between-group difference = 17.0%; 95% CI, 6.2 to 28.2).

In the ITC for JAK inhibitor–naïve patients, the results suggested that at week 24, treatment with fedratinib 400 mg once daily was associated with slightly greater proportion of patients achieving a 35% or greater reduction in spleen volume compared with ruxolitinib (between-group difference = 12.3%; 95% CI, 0.6 to 24.0). The results also suggested that there was no difference between fedratinib and ruxolitinib in achieving a 50% or greater reduction in TSS from baseline to week 24 (between-group difference = -9.4%; 95% CI, -23.9 to 5.2).

In both ITCs, harms outcomes of fedratinib were descriptively summarized; therefore, no firm conclusions can be made for harm outcomes from the ITCs.

Key limitations to the ITCs included concerns that not all effect modifiers and prognostic factors, which were essential in the matching-adjusted indirect comparison and simulated treatment comparison to ensure balance and reduce bias, were identified and adjusted for in the analyses. There is substantial risk of bias in the ITC results, thus they should be interpreted with caution.

Cost and Cost-Effectiveness

Fedratinib is available as a 100 mg capsule at a submitted price of \$84.39 per capsule. The recommended dosage is 400 mg once daily for patients with a baseline platelet count of $50 \times 10^9/L$ or greater. The 28-day drug acquisition cost of fedratinib is \$9,452 per patient.

The sponsor submitted a stratified cost-utility analysis to assess the cost-effectiveness of fedratinib among 2 subgroups: patients without prior exposure to JAK inhibitors (JAK inhibitor-naïve patients) and patients previously exposed to ruxolitinib (ruxolitinib-experienced patients). Fedratinib was compared with ruxolitinib and BAT in the JAK inhibitor-naïve subgroup and to BAT in the ruxolitinib-experienced subgroup. The composition of BAT differed depending on the subgroup and number of prior JAK inhibitors used. The analysis was undertaken from the perspective of a Canadian publicly funded health care payer over a lifetime time horizon.

A discrete event simulation was submitted in which patients had their disease trajectories separately tracked. Movement through the model was based on an individual's treatment response, time to treatment discontinuation, duration of treatment response, progression to acute myeloid leukemia, and overall survival. After 24 weeks of treatment, treatment response was defined as a 35% or greater reduction in spleen volume; those with less than 35% were assumed to discontinue JAK inhibitor treatment and to switch to BAT (in which ruxolitinib was included within the composition of BAT). Direct comparative evidence for the proportion of patients achieving a treatment response exists only for fedratinib compared with BAT in the JAK inhibitor-naïve subgroup; the other comparisons were informed by the sponsor's commissioned ITCs and naïve comparisons.

The following key limitations were identified:

- The comparative clinical efficacy of fedratinib is highly uncertain because there is no direct head-to-head evidence comparing fedratinib and ruxolitinib in the JAK inhibitor-naïve subgroup or comparing fedratinib and BAT in the ruxolitinib-experienced subgroup. Substantial uncertainty exists in the results of the sponsor's ITCs.
- The submitted pharmacoeconomic analysis does not adequately reflect the clinical management of myelofibrosis patients because treatment decisions in clinical practice are not based solely on spleen volume and a threshold of 35% reduction is not typically used.
- The comparator, defined as BAT, included a majority of treatments not used in the treatment of myelofibrosis in Canada.
- The long-term extrapolation of the effects of fedratinib, including overall survival, duration of treatment response, and time to discontinuation, is highly uncertain. The predicted overall survival for fedratinib was overestimated according to the clinical experts consulted by CADTH.
- Thiamine testing is not uniformly reimbursed publicly across Canadian jurisdictions and may be paid out-of-pocket by patients.

CADTH undertook reanalyses to address the identified limitations, including redefining treatment response in terms of symptom and spleen response, revising the composition of the BAT comparator, adopting an alternative parametric distribution of fedratinib overall survival, and removing the cost of thiamine testing. CADTH was unable to address the lack of comparative clinical data for fedratinib versus ruxolitinib for the JAK inhibitor-naïve subgroup or for fedratinib versus BAT for the ruxolitinib-experienced subgroup. As such, the

CADTH base case was limited to the JAK inhibitor–naive subgroup and only included pairwise comparisons of fedratinib and BAT.

Based on CADTH reanalyses, fedratinib is not cost-effective at a \$50,000 willingness-to-pay threshold for JAK inhibitor–naive patients compared with BAT if patients are assumed to be eligible to receive ruxolitinib as part of BAT after discontinuation of fedratinib (ICER: \$416,446 per QALY gained). In a CADTH scenario analysis of JAK inhibitor–naive patients, when ruxolitinib is removed as part of BAT, the ICER for fedratinib versus BAT is \$88,698 per QALY gained.

pERC Committee Members

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April 15, 2021 Meeting

Regrets: None

Conflicts of Interest: None