Provisional Funding Algorithm

Indication: Myelofibrosis

Please always check Provisional Funding Algorithms to ensure you are reading the most recent algorithm report.

Background

Following a request from jurisdictions, Canada's Drug Agency (CDA-AMC) may design or update an algorithm depicting the sequence of funded treatments for a particular tumour type. These algorithms are proposals for the jurisdictions to implement and adapt to the local context. As such, they are termed "provisional." Publishing of provisional algorithms is meant to improve transparency of the oncology drug funding process and promote consistency across jurisdictions.

Provisional funding algorithms are based on 3 principal sources of information:

- pan-Canadian Oncology Drug Review Expert Review Committee (pERC) reimbursement recommendations and/or implementation guidance regarding drug place in therapy and sequencing
- implementation advice from panels of clinicians convened by CDA-AMC concerning sequencing of drugs in the therapeutic space of interest
- existing oncology drug reimbursement criteria and legacy funding algorithms adopted by jurisdictional drug plans and cancer agencies.

Note that provisional funding algorithms are not treatment algorithms; they are neither meant to detail the full clinical management of each patient nor the provision of each drug regimen. The diagrams may not contain a comprehensive list of all available treatments, and some drugs may not be funded in certain jurisdictions. All drugs are subject to explicit funding criteria,

which may also vary between jurisdictions. Readers are invited to refer to the cited sources of information on the CDA-AMC website for more details.

Provisional funding algorithms also delineate treatment sequences available to patients who were never treated for the condition of interest (i.e., incident population). Time-limited funding of new options for previously or currently treated patients (i.e., prevalent population) is not detailed in the algorithm.

Provisional funding algorithms may contain drugs that are under consideration for funding. Algorithms will not be dynamically updated by CDA-AMC following changes to drug funding statuses. Revisions and updates will occur only upon request by jurisdictions.

Jurisdictional cancer drug programs requested a CDA-AMC Provisional Funding Algorithm on myelofibrosis. However, no outstanding implementation issues were identified, and no additional implementation advice is provided in this report. The algorithm depicted herein is meant to reflect the current and anticipated funding landscape based on the previously mentioned sources of information.

History and Development of the Provisional Funding Algorithm

This is the first development of a rapid provisional funding algorithm for myelofibrosis to incorporate reimbursement recommendations for momelotinib, fedratinib and ruxolitinib

Table 1: Relevant Previous Recommendations

Generic name (brand name)	Date of recommendation	Recommendation and guidance on treatment sequencing
Momelotinib (Ojjaara)	TBD	The CDA-AMC pCODR Expert Review Committee (pERC) recommends that momelotinib be reimbursed for the treatment of splenomegaly and/or disease-related symptoms, in adult patients with intermediate or high-risk myelofibrosis (MF), post polycythemia vera MF or post essential thrombocythemia MF who have moderate to severe anemia, only if the following conditions are met. **Initiation** 1. Momelotinib should be initiated in adult patients, with or without prior treatment experience with a JAKI, who have primary MF, post-polycythemia vera MF, or post-essential thrombocythemia MF who meet all of the following criteria: 1.1. high-risk or intermediate-2 risk MF defined by the DIPSS or intermediate-1 risk associated with symptomatic splenomegaly and/or hepatomegaly; AND 1.2. palpable splenomegaly of at least 5 cm

Generic name (brand name)	Date of recommendation	Recommendation and guidance on treatment sequencing
		1.3. moderate to severe anemia, defined by a hemoglobin level less than 100 g/L. 2. Patients must have good performance status. **Renewal** 3. Patients should be assessed for a response to treatment with momelotinib every 3 to 6 months. **Discontinuation** 4. Treatment with momelotinib should be discontinued upon occurrence of any of the following: 4.1. response to treatment has not been demonstrated after 6 months of treatment 4.2. disease progression 4.3. development of serious adverse events or unacceptable toxicity **Prescribing** 5. Momelotinib should be prescribed under the care of a clinician with expertise in treating and managing MF. **Pricing** 6. The price of momelotinib should be negotiated so that it does not exceed the drug program cost of treatment with the least costly JAKi reimbursed for the treatment of MF. **Guidance on Sequencing** • The clinical experts indicated that the use of momelotinib would likely be prioritized for patients with myelofibrosis who are anemic or borderline anemic. The clinical experts highlighted the importance of carefully considering the threshold for anemia, particularly for patients with mild anemia (hemoglobin levels between 100 g/L and 120 g/L). Momelotinib could be particularly beneficial in cases where treatment with ruxolitinib has led to anemia. pERC agreed with the experts, but noted that the evidence for patients with anemia was limited to those

Generic name (brand name)	Date of recommendation	Recommendation and guidance on treatment sequencing
		with moderate to severe anemia (hemoglobin levels less than or equal to 100 g/L). • The experts indicated that while there is no direct evidence for downstream treatment options following progression on momelotinib, other JAK inhibitors like fedratinib may be considered as a subsequent line of therapy for patients with myelofibrosis for whom ruxolitinib is contraindicated or for patients who cannot tolerate ruxolitinib. The experts indicated that momelotinib could be used as a first-line treatment, with fedratinib as a potential second-line option. In cases where the primary concern is anemia rather than splenomegaly, momelotinib might be more suitable in third-line settings. However, the experts acknowledged that the evidence is limited, and treatment decisions should be individualized based on patient response and specific clinical scenarios. pERC acknowledged that treatment decisions are individualized based on the symptomatic treatment needs. However, pERC noted that treatment options following progression on ruxolitinib are limited, and that no evidence was identified for the use of fedratinib following progression on momelotinib.
Fedratinib (Inrebic)	June 21, 2021	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 following conditions are met: **Initiation** 1. Fedratinib should be initiated in patients for whom ruxolitinib is contraindicated or patients who are intolerant of ruxolitinib.

Generic name (brand name)	Date of recommendation	Recommendation and guidance on treatment sequencing
		2. Fedratinib should not be reimbursed in patients who experience disease progression following treatment with ruxolitinib. 3. Patients must have good performance status. **Renewal** 1. Patients should be assessed for a response to treatment with fedratinib every 3 to 6 months. 2. A response to treatment with fedratinib is defined as either of the following based on clinical assessment: • evidence of reduction in spleen size • symptom improvement. **Discontinuation** 1. Treatment with fedratinib should be discontinued in patients who demonstrate any 1 of the following: • progressive increase in spleen size • return of constitutional symptoms • development of serious adverse events. **Prescribing** 1. The patient should be under the care of a clinician with expertise in treating and managing myelofibrosis. 2. Fedratinib should not be prescribed in combination with other JAK inhibitors or other therapies. **Pricing** 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.
Ruxolitinib (Jakavi)	January 14, 2013	The pCODR Expert Review Committee (pERC) recommends funding ruxolitnib (Jakvi) conditional on the cost-effectiveness of ruxolitinib being improved to an acceptable

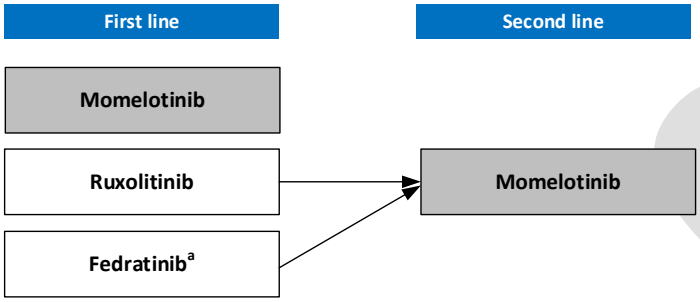
Generic name (brand name)	Date of recommendation	Recommendation and guidance on treatment sequencing
		level. Ruxolinitib should be funded for patients with intermediate to high risk symptomatic Myelofibrosis as assessed using the Dynamic International Prognostic Scoring System (DIPSS) Plus or patients with symptomatic splenomegaly. Patients should have an ECOG performance status ≤ 3 and be either previously untreated or refractory to other treatment.

DIPSS = Dynamic International Prognostic Scoring System; ECOG = Eastern Cooperative Oncology Group, Hgb = hemoglobin; JAKi = Janus kinase inhibitor; MF = myelofibrosis; pCODR = pan-Canadian Oncology Drug Review; RBC = red blood cell

Provisional Funding Algorithm

Figure 1: Provisional Funding Algorithm Diagram for Myelofibrosis

Alt Text: The funded options for myelofibrosis include momelotinib, fedratinib and ruxolitinib.



- Note that these options are for adult patients with intermediate or high risk primary myelofibrosis, post-polycythemia vera myelofibrosis or post-essential thrombocythemia myelofibrosis.
- Risk assessment is based on Dynamic information prognostic scoring system (DIPSS)

[a] Note that fedratinib should be initiated in patients for whom ruxolitinib is contraindicated or patients who are intolerant of ruxolitinib. Fedratinib should not be reimbursed in patients who experience disease progression following treatment with ruxolitinib.

Therapy funded across most jurisdictions	Therapy under review for funding (pCPA or province/cancer agency)

Description of the Provisional Funding Algorithm

Myelofibrosis

For patients with intermediate or high-risk primary myelofibrosis, post-polycythemia vera myelofibrosis or post-essential thrombocythemia myelofibrosis, the funded options may include momelotinib, ruxolitinib or fedratinib.

Momelotinib would likely be prioritized for patients with myelofibrosis who are anemic or borderline anemic.

Note that fedratinib should be initiated in patients for whom ruxolitinib is contraindicated or patients who are intolerant of ruxolintib. Fedratinib should not be reimbursed in patients who experience disease progression following treatment with ruxolinitib.

Following progression on ruxolinitib or fedratinib, momelotinib may be funded if the patient meets the eligibility criteria.

Additional Remarks

TBD