Technology Guidance

Momelotinib

for treating myelofibrosis in patients with moderate to severe anaemia

Technology Guidance from the MOH Drug Advisory Committee

Guidance Recommendations

The Ministry of Health's Drug Advisory Committee has recommended:

- ✓ Momelotinib 100 mg, 150 mg and 200 mg tablets for treating myelofibrosis-related splenomegaly or symptoms in patients with moderate to severe anaemia.

Funding status

Momelotinib 100 mg, 150 mg and 200 mg tablets are recommended for inclusion on the Medication Assistance Fund (MAF) for the abovementioned indication from 1 April 2026.

Clinical indication, subsidy class and MediShield Life claim limit for momelotinib are provided in the Annex.

Updated: 6 February 2026

Company-led submission

1.1. At the June 2025 meeting, the MOH Drug Advisory Committee ("the Committee") considered the technology evaluation of momelotinib for treating myelofibrosis (MF)-related splenomegaly or symptoms in patients with moderate to severe anaemia. The evaluation included the company's evidence submission and a review by one of ACE's evidence review centres.

1.2. Expert opinion obtained from clinicians from public healthcare institutions, the MOH Cancer Drug Subcommittee, and patient experts from local patient and voluntary organisations, assisted ACE in ascertaining the clinical value of momelotinib.

1.3. The evidence was used to inform the Committee's deliberations around four core decision-making criteria:

- Clinical need of patients and nature of the condition;
- Clinical effectiveness and safety of the technology;
- Cost effectiveness (value for money) – the incremental benefit and cost of the technology compared to existing alternatives; and
- Estimated annual technology cost and the number of patients likely to benefit from the technology.

1.4. Additional factors, including social and value judgments, may also inform the Committee's funding considerations.

Clinical need

2.1. MF is a myeloproliferative neoplasm characterised by the progressive replacement of normal bone marrow with fibrous tissue, leading to impaired blood cell production. In Singapore, approximately 123 patients are living with MF, and more than half of these patients will develop moderate to severe anaemia (haemoglobin <100g/L) due to their disease. Anaemia is a key prognostic factor in MF and patients with moderate to severe anaemia have particularly poor outcomes.

2.2. The Committee noted that momelotinib is a Janus kinase inhibitor (JAKi) that targets activin A receptor type 1 (ACVR1) in addition to JAK. The effect on ACVR1 may improve anaemia by restoring iron homeostasis and increasing erythropoiesis. For patients with MF and moderate to severe anaemia, the Committee agreed that momelotinib is likely to replace ruxolitinib or fedratinib in JAKi-naïve patients, and ruxolitinib or fedratinib in combination with an erythropoiesis-stimulating agent (ESA) and/or danazol in JAKi-experienced patients. The Committee noted that utilisation of the most commonly used JAKi ruxolitinib seems to have plateaued, while the usage of fedratinib has increased significantly since it was subsidised for treating MF in 2024.

2.3. The Committee considered a testimonial from a local patient about their lived experience with MF and the treatments they have received. The Committee noted that MF had negatively impacted the patient's ability to perform daily activities due to fatigue and breathlessness. The patient was being treated with ruxolitinib and felt that it worked well and was convenient to take. However, the patient experienced side effects, particularly worsening of anaemia despite receiving weekly epoetin beta injections. The patient highlighted that there were limited treatment options available and expressed concern about the financial burden of treatment costs.

2.4. The Committee acknowledged that the patient was unfamiliar with momelotinib but would be willing to accept the side effects of a new treatment if it improved symptoms without incurring higher costs. Overall, the patient considered that any new treatment for MF should maintain a healthy blood count, improve quality of life for patients and carers, allow them to spend more time with family and friends, and be more affordable.

Clinical effectiveness and safety

3.1. The Committee reviewed the clinical evidence in the company's submission from three phase III randomised controlled trials:

- SIMPLIFY-1: A double-blind, non-inferiority trial comparing momelotinib with ruxolitinib in JAKi-naïve patients.
- SIMPLIFY-2: An open-label, superiority trial comparing momelotinib with best available therapy (BAT) in JAKi-experienced patients.
- MOMENTUM: A double-blind, superiority trial comparing momelotinib with danazol in JAKi-experienced patients.

The Committee considered the MOMENTUM trial results as supplementary evidence as danazol is not widely used in Singapore.

3.2. For JAKi-naïve patients, SIMPLIFY-1 demonstrated that momelotinib was non-inferior to ruxolitinib for the primary endpoint of splenic response rate (SRR) but failed to meet non-inferiority for total symptom score response (TSS), although this may be attributed to trial design limitations including higher baseline TSS in the momelotinib group versus ruxolitinib and the handling of missing data. The Committee considered the numerical improvements in transfusion-related outcomes to be exploratory since momelotinib failed to demonstrate non-inferiority with ruxolitinib for the secondary endpoint of TSS in the statistical hierarchy of testing. Similar results were observed in a post-hoc analysis of the subgroup with moderate to severe anaemia (Table 1).

Table 1: SIMPLIFY-1 trial efficacy results at Week 24 (ITT population; randomised phase)

Outcome	Momelotinib	Ruxolitinib
ITT population		
Primary endpoint – SRR ≥35%		
Responder, n/N (%)	57/215 (26.5%)	64/217 (29.5%)
Non-inferior difference (95% CI) [a]	**0.09 (0.02, 0.16), p = 0.014**	
Secondary endpoint – Response rate in MPN-SAF TSS reduction ≥50%		
Responder, n/N (%)	60/211 (28.4%)	89/211 (42.2%)
Non-inferior difference (95% CI) [b]	0.00 (−0.08, 0.08), p = 0.98	
Secondary endpoint – Transfusion-related outcomes [c]		
RBC transfusions [d] (mean units/patient month [95% CI])	0.4 (0.3, 0.6)	1.5 (1.1, 2.2)
Difference	0.28 (0.19, 0.43)	
Hgb <100g/L subgroup		
Primary endpoint – SRR ≥35%		
Responder, n/N (%)	27/86 (31.4%)	31/94 (33.0%)
Non-inferior difference (95% CI)	**0.13 (0.01, 0.24), p = 0.029**	
Secondary endpoint – Response rate in MPN-SAF TSS reduction ≥50%		
Responder, n/N (%)	21/86 (25.0%)	33/94 (35.5%)
Non-inferior difference (95% CI)	-0.12 (-0.26, 0.02), p = 0.11	
Secondary endpoint – Transfusion-related outcomes [c]		
RBC transfusions [d] (mean units/patient month [95% CI])	0.8 (0.6, 1.2)	1.8 (1.3, 2.5)
Difference	0.46 (0.30, 0.71)	

Abbreviations: CI, confidence interval; Hgb, haemoglobin; ITT, intention to treat; MPN-SAF, Myeloproliferative Neoplasm Symptom Assessment Form; n, number of participants with event; N, total participants in group; RBC, red blood cell; SRR, splenic response rate; TSS, total symptom score.

Bold indicates statistically significant difference.

[a] Non-inferiority for splenic response was calculated as momelotinib response rate – 0.6 × ruxolitinib response rate. If the lower bound of the 2-sided 95% CI (calculated based on stratum-adjusted Cochran-Mantel-Haenszel proportion) was greater than 0, the momelotinib group would be non-inferior to the ruxolitinib group for this outcome.

[b] Non-inferiority for TSS was calculated as momelotinib response rate – 0.67 × ruxolitinib response rate. If the lower bound of the 2-sided 95% CI (calculated based on stratum-adjusted Cochran-Mantel-Haenszel proportion) was greater than 0, the momelotinib group would be non-inferior to the ruxolitinib group for this outcome.

[c] As non-inferiority was not achieved in TSS response – the first secondary endpoint in the hierarchy of statistical testing – subsequent endpoints including transfusion-related outcomes were not formally tested for statistical significance and should be considered exploratory.

[d] Rate of RBC transfusions is defined as the average number of RBC units transfused per patient-month during the double-blind phase. The difference between treatment arms is the rate ratio of RBC transfusions (95% CI, negative binomial model adjusted for strata).

3.3. Regarding safety, patients receiving momelotinib had higher rates of treatment-emergent adverse events (TEAEs) leading to discontinuation compared to ruxolitinib (12.6% vs 5.6%) but lower rates of TEAEs leading to dose reduction or interruption (18.2% vs 36.6%).

3.4. The submission described momelotinib as non-inferior in terms of effectiveness and safety compared to ruxolitinib in JAK-naïve patients with MF and moderate to severe anaemia. Based on the evidence submitted, the Committee agreed that these claims were reasonable. However, they considered that the submission's claim of transfusion benefits with momelotinib versus ruxolitinib was not adequately supported.

3.5. The submission did not present any comparative efficacy evidence for momelotinib versus fedratinib in JAKi-naïve patients. Hence, the Committee considered the comparative efficacy of momelotinib with fedratinib remains uncertain. For safety outcomes, the submission presented an unanchored matching-adjusted indirect comparison (MAIC) that used data from the SIMPLIFY-1 (momelotinib) and JAKARTA (fedratinib) trials to suggest a favourable safety profile for momelotinib. However, due to inherent limitations in the unanchored MAIC, the Committee agreed that momelotinib may be considered to have a safety profile that is at least non-inferior to fedratinib.

3.6. For JAKi-experienced patients, the Committee noted the limited applicability of evidence from SIMPLIFY-2, as only 6% of patients in the comparator arm (BAT) received a JAKi in combination with an ESA and/or danazol. These treatments are commonly used in local clinical practice for these patients.

3.7. Based on the submitted evidence, the Committee agreed that the comparative efficacy and safety for momelotinib versus ruxolitinib and fedratinib, in combination with an ESA and/or danazol, remains uncertain.

3.8. The Committee acknowledged that SIMPLIFY-2 only included patients in the post-ruxolitinib setting, but considered the company's requested listing, which included patients who received other JAKis such as fedratinib, to be reasonable. They considered the safety and efficacy of momelotinib would likely be comparable regardless of which specific JAKi had been previously administered, and noted that this positioning aligned with overseas HTA agencies such as Canada's Drug Agency. However, the Committee agreed that the listing criteria should be restricted to patients with intermediate or high-risk MF, in line with the patient populations in pivotal trials (SIMPLIFY-1, SIMPLIFY-2).

Cost effectiveness

4.1. The Committee reviewed the submission's cost-minimisation analyses (CMAs) comparing momelotinib with the nominated comparators in both JAKi-naïve and JAKi-experienced populations.

4.2. While the submission's CMA results suggested potential cost savings with momelotinib versus all comparators, the Committee considered these analyses highly uncertain due to several limitations:

- The non-inferiority claim between momelotinib and fedratinib was uncertain due to a lack of comparative efficacy data.
- Limited applicability of SIMPLIFY-2 results to the management of local JAKi-experienced patients.
- Estimation of equi-effective doses based on clinician estimates of the distribution of dosing regimens in local practice, instead of using mean doses from clinical trials.
- Inclusion of red blood cell transfusion rates and their associated costs between treatments, even though transfusion-related outcomes were exploratory.
- Incorporation of grade ≥3 adverse event (AE) management costs, despite clinical evidence showing that a non-inferiority safety claim was more reasonable.

4.3. Given these uncertainties, the Committee considered that a revised analysis incorporating drug costs only was more appropriate. The evidence review centre conducted the revised analysis using mean doses for momelotinib (188.4 mg/day), ruxolitinib (28.0 mg/day) and fedratinib (377.2 mg/day). Mean doses for momelotinib and ruxolitinib were derived from SIMPLIFY-1, while the dose for fedratinib was derived from JAKARTA, taking into account relative dose intensity. Based on the revised analysis, the Committee noted that the total treatment cost of momelotinib was higher than that of ruxolitinib and fedratinib.

4.4. The Committee therefore considered that, at the proposed price, momelotinib did not represent an acceptable use of healthcare resources for treating MF-related splenomegaly or symptoms in patients with moderate to severe anaemia.

Estimated annual technology cost

5.1. Using an epidemiological approach, the submission estimated that the annual cost impact to the public healthcare system would be between SG$1 million and SG$3 million over the first five years of listing momelotinib on the MOH List of Subsidised Drugs for treating MF in patients with moderate to severe anaemia. The annual expenditure is expected to decrease over the first few years, with a higher initial expenditure due to the use of momelotinib in a prevalent pool of patients, in addition to use in incident patients.

5.2. The Committee considered that the submission's estimates and price-volume agreement (PVA) caps were high, due to an overestimation of eligible patients, optimistic uptake rates, an assumption of treatment durations beyond mean trial durations, and not incorporating mean doses used in the trials. Based on the revised budget impact model, the annual cost impact to the public healthcare system was estimated to decrease from between SG$1 million and SG$3 million in the first year of listing to less than SG$1 million in the fifth year of listing.

Recommendations (June 2025)

6.1. Based on the evidence submitted, the Committee recommended not listing momelotinib on the MOH List of Subsidised Drugs for treating MF-related splenomegaly or symptoms in patients with moderate to severe anaemia. This decision was based on momelotinib being unlikely to represent an acceptable use of healthcare resources at the price proposed by the company.

Updated recommendations (November 2025)

7.1. Following a negative recommendation by the Committee at the June 2025 meeting, the company of momelotinib submitted a revised pricing proposal for funding consideration.

7.2. Based on the revised proposal, the Committee considered momelotinib to be an acceptable use of healthcare resources for treating myelofibrosis in patients with moderate to severe anaemia. Hence, the Committee recommended momelotinib 100 mg, 150 mg and 200 mg tablets be listed on the Medication Assistance Fund (MAF) for this indication.

ANNEX

Recommendations by the MOH Drug Advisory Committee

Drug preparation	Approved clinical indication	Subsidy class (implementation date)	MediShield Life claim limit per month (implementation date)
Momelotinib 100 mg, 150 mg and 200 mg tablets	For the treatment of disease-related splenomegaly or symptoms in patients with moderate to severe anaemia who have intermediate- or high-risk myelofibrosis (MF), including primary MF, post-polycythaemia vera MF, or post-essential thrombocythaemia MF, and who are Janus Kinase inhibitor (JAKi)-naive or JAKi-experienced.	MAF (1 Apr 2026)	$2,000 (1 Apr 2026)

Abbreviations: MAF, Medication Assistance Fund.

VERSION HISTORY

Guidance on momelotinib for treating myelofibrosis in patients with moderate to severe anaemia

This Version History is provided to track any updates or changes to the guidance following the first publication date. It is not part of the guidance.

1. **Publication of guidance**

   Date of Publication 2 Sep 2025

2. **Guidance updated to reflect the inclusion of momelotinib on the MAF and its MediShield Life claim limit**

   Date of Publication 6 Feb 2026

Agency for Care Effectiveness - ACE Agency for Care Effectiveness (ACE)

About the Agency

The Agency for Care Effectiveness (ACE) was established by the Ministry of Health (Singapore) to drive better decision-making in healthcare through health technology assessment (HTA), clinical guidance, and education.

As the national HTA agency, ACE conducts evaluations to inform government funding decisions for treatments, diagnostic tests and vaccines, and produces guidance for public hospitals and institutions in Singapore.

The guidance is not, and should not be regarded as, a substitute for professional or medical advice. Please seek the advice of a qualified healthcare professional about any medical condition. The responsibility for making decisions appropriate to the circumstances of the individual patient remains with the healthcare professional.

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