Technology Guidance

Ruxolitinib

for treating polycythaemia vera

Technology Guidance from the MOH Drug Advisory Committee

Guidance Recommendations

The Ministry of Health's Drug Advisory Committee has not recommended ruxolitinib 5 mg tablet for listing on the Medication Assistance Fund (MAF) for treating patients with polycythaemia vera who are resistant to or intolerant of hydroxyurea, in view of low clinical need, and uncertain clinical and cost-effectiveness compared with subsidised alternatives.

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

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Factors considered to inform the recommendations for subsidy

Technology evaluation

1.1. The MOH Drug Advisory Committee ("the Committee") considered the evidence presented for the technology evaluation of ruxolitinib for treating polycythaemia vera (PV). The Agency for Care Effectiveness (ACE) conducted the evaluation in consultation with clinical experts from the public healthcare institutions. Published clinical and economic evidence for ruxolitinib was considered in line with its registered indication. Additional expert opinion was obtained from the MOH Oncology Drug Subcommittee (ODS) who assisted ACE to ascertain the clinical value of ruxolitinib for PV and provided clinical advice on its appropriate and effective use based on the available clinical evidence.

1.2. The 10 mg strength of ruxolitinib was excluded from evaluation as it was not commercially available in Singapore at the time of evaluation.

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 subsidy considerations.

Clinical need

2.1 Polycythaemia vera (PV) is a myeloproliferative neoplasm that is characterised by the overproduction of blood cells and platelets. Patients with PV are prone to developing blood clots that might lead to major complications such as heart attack, deep vein thrombosis, and stroke.

2.2 In local clinical practice, patients receive hydroxyurea as first-line treatment in line with international clinical practice guidelines. Peginterferon alfa-2a or ruxolitinib are considered for patients who require subsequent treatment due to an inadequate response or loss of response to hydroxyurea. The Committee heard that both hydroxyurea and peginterferon alfa-2a are included in the MOH List of Subsidised Drugs and considered that there was low clinical need to subsidise ruxolitinib.

Clinical effectiveness and safety

3.1 The Committee reviewed the available evidence for ruxolitinib from two randomised controlled trials (RCTs; RESPONSE and RESPONSE 2) which were conducted in patients who were unsuitable for hydroxyurea due to inadequate response or unacceptable side effects.

3.2 Results from RESPONSE showed that ruxolitinib was superior to best available therapy (BAT; i.e., primarily hydroxyurea, interferon, or no therapy) in achieving haematocrit control and reducing splenomegaly in patients with PV. However, five-year overall survival (OS) for ruxolitinib and BAT were comparable (hazard ratio [HR] 0.95; 95% CI 0.38 to 2.41). In RESPONSE 2, ruxolitinib showed a statistically significant improvement in haematocrit control compared to BAT.

3.3 In terms of safety, ruxolitinib had a different safety profile compared with BAT and was associated with more anaemia and weight gain while BAT was associated with more thrombocytopenia and fatigue. Overall, discontinuation rates of ruxolitinib due to AEs were low in both trials.

Cost effectiveness

4.1 The manufacturer of ruxolitinib was invited to submit a value-based pricing (VBP) proposal for their product for subsidy consideration. In the absence of a local cost-effectiveness analysis, the Committee reviewed evaluations from overseas HTA agencies. They noted that ruxolitinib was not recommended for funding by the PBAC (Australia) due to uncertain clinical and cost effectiveness, while CADTH (Canada) only supported funding if cost-effectiveness was improved to an acceptable level. Based on the manufacturer's proposal, the Committee agreed that ruxolitinib was unlikely to be cost-effective at the proposed price for treating PV.

Estimated annual technology cost

5.1 Based on local epidemiological rates and estimated drug utilisation in the public healthcare institutions, the annual cost impact in the first year of listing ruxolitinib on MAF for treating patients with PV who are resistant to, or intolerant of hydroxyurea was estimated to be less than SG$1 million. However, the Committee was concerned with the budget uncertainty associated with a potentially long and unknown treatment duration for PV in the subsequent years.

Recommendations

6.1. Based on available evidence, the Committee recommended not listing ruxolitinib on the MAF for treating patients with PV who are resistant to, or intolerant of hydroxyurea, in view of low clinical need and uncertain clinical and cost-effectiveness compared with subsidised alternatives.

Annex

Recommendations by the MOH Drug Advisory Committee

Drug preparation	Clinical indications	Subsidy class	MediShield Life claim limit per month
Ruxolitinib 5 mg tablet	Treatment of patients with polycythaemia vera who are resistant or intolerant to hydroxyurea.	Not recommended for subsidy	Not recommended for MediShield Life claims