Technology Guidance

Polatuzumab vedotin

for treating relapsed or refractory diffuse large B-cell lymphoma

Technology Guidance from the MOH Drug Advisory Committee

Guidance Recommendations

The Ministry of Health's Drug Advisory Committee has not recommended listing polatuzumab vedotin on the Medication Assistance Fund (MAF) for treating patients with relapsed or refractory diffuse large B-cell lymphoma who are not eligible for haematopoietic cell transplant due to low clinical need, uncertain clinical effectiveness and unfavourable cost-effectiveness at the price proposed by the manufacturer.

Clinical indication, subsidy class and MediShield Life claim limit for polatuzumab vedotin 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 polatuzumab vedotin ("polatuzumab") for treating relapsed or refractory diffuse large B-cell lymphoma (DLBCL). 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 polatuzumab was considered in line with its registered indication. Additional expert opinion was obtained from the MOH Oncology Drug Subcommittee (ODS) who assisted ACE ascertain the clinical value of polatuzumab and provided clinical advice on its appropriate and effective use based on the available clinical evidence.

1.2. 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.

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

Clinical need

2.1. DLBCL is the most common type of non-Hodgkin lymphoma (NHL), accounting for almost half of all NHL diagnoses. In Singapore, approximately 300 patients are diagnosed with DLBCL each year. Local clinical experts confirmed that although many patients can be cured with 6-8 cycles of rituximab in combination with cyclophosphamide, doxorubicin, vincristine and prednisone (R-CHOP), 30-40% of patients experience relapse or have primary refractory disease and require subsequent treatment.

2.2. In local practice, patients with relapsed or refractory DLBCL who are not eligible for haematopoietic cell transplant are typically treated with gemcitabine and platinum-based chemotherapy regimens. In view of the number of chemotherapy regimens that are already subsidised for these patients, the Committee considered that the clinical need for an additional subsidised regimen was low.

2.3. The Committee also heard that polatuzumab was being investigated in patients with

previously untreated DLBCL in a randomised controlled trial (POLARIX), hence, there may be potential changes to its place in therapy over time.

Clinical effectiveness and safety

3.1. The Committee reviewed the available clinical evidence for polatuzumab from the pivotal randomised controlled trial (GO29365) in patients with relapsed or refractory DLBCL who were not eligible for haematopoietic cell transplant. The Committee noted that while trial results showed that polatuzumab in combination with bendamustine and rituximab significantly improved progression-free survival and overall survival compared with bendamustine and rituximab alone, these results were likely to be confounded in favour of the polatuzumab arm, as patients in the comparator arm were likely to have a poorer prognosis.

3.2. As the comparator arm in the trial was not reflective of local practice, the Committee considered the comparative effectiveness of the polatuzumab combination regimen was unknown versus relevant comparators used in local practice (such as rituximab + gemcitabine + dexamethasone + cisplatin (R-GDP) and rituximab + gemcitabine + oxaliplatin (R-GemOx)). The ongoing phase III randomised controlled trial (POLARGO) would provide more evidence to assess the clinical effectiveness of polatuzumab compared with a relevant comparator (R-GemOx) for treating relapsed or refractory DLBCL.

3.3. In terms of safety, the Committee noted that polatuzumab in combination with bendamustine and rituximab was associated with more Grade ≥3 adverse events (AEs) compared with bendamustine and rituximab alone. The most commonly reported Grade ≥3 AEs associated with polatuzumab use were neutropenia and thrombocytopenia.

Cost effectiveness

4.1. The manufacturer of polatuzumab was invited to submit a value-based pricing (VBP) proposal for subsidy consideration. In the absence of a local cost-effectiveness analysis, the Committee reviewed evaluations from overseas HTA agencies. They noted that the drug costs used in the evaluations were not published or had included confidential discounts from manufacturers. Therefore, it was unknown whether the prices were comparable to local prices and if the results were generalisable to the Singapore context.

4.2. The Committee noted that at the proposed price, the treatment cost of polatuzumab in combination with bendamustine and rituximab was substantially higher than the cost of standard of care chemotherapy regimens for relapsed or refractory DLBCL. Given the limitations in the clinical data and substantial price premium compared with

standard of care treatment regimens, the Committee concluded that polatuzumab in combination with bendamustine and rituximab did not represent a cost-effective use of healthcare resources.

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 polatuzumab on the MAF for treating relapsed or refractory DLBCL was estimated to be between SG$3 million to less than SG$5 million.

Recommendations

6.1. Based on available evidence, the Committee recommended not listing polatuzumab on the MAF for treating relapsed or refractory DLBCL due to low clinical need, uncertain clinical effectiveness and unfavourable cost-effectiveness at the price proposed by the manufacturer.

ANNEX

Recommendations by the MOH Drug Advisory Committee

Drug preparation	Clinical indications	Subsidy class	MediShield Life claim limit per month
Polatuzumab vedotin 140 mg powder for concentrate for solution for infusion	Polatuzumab vedotin in combination with bendamustine and rituximab for the treatment of patients with relapsed or refractory diffuse large B-cell lymphoma who are not eligible for haematopoietic cell transplant	Not recommended for subsidy	Not recommended for MediShield Life claims

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 subsidy decisions for treatments, diagnostic tests and vaccines, and produces guidance for public hospitals and institutions in Singapore.

This guidance is based on the evidence available to the MOH Drug Advisory Committee as at 27 May 2021. It 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.

Find out more about ACE at www.ace-hta.gov.sg/about

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