Technology Guidance

# Maribavir

## for treating refractory or drug-intolerant cytomegalovirus infection after transplant

**Technology Guidance from the MOH Drug Advisory Committee**

## Guidance Recommendations

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

- ✓ Maribavir 200 mg tablet for treating post-transplant cytomegalovirus infection or disease in adults who are refractory (with or without genotypic resistance) or intolerant to prior antiviral therapy.

### Funding status

Maribavir 200 mg tablet is recommended for inclusion on the Medication Assistance Fund (MAF) for the abovementioned indication from 1 September 2026.

Maribavir should be used in line with the additional clinical criteria listed in the Annex.

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## Technology evaluation

1.1. At the April 2026 meeting, the MOH Drug Advisory Committee ("the Committee") considered the evidence presented for the technology evaluation of maribavir, for treating post-transplant cytomegalovirus (CMV) infection/disease in adults who are refractory, with or without genotypic resistance, or intolerant to prior antiviral therapy. The Agency for Care Effectiveness (ACE) conducted the evaluation in consultation with clinical experts from public healthcare institutions (PHIs). Published clinical and economic evidence for maribavir was considered in line with its registered indication.

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 funding considerations.

## Clinical need

2.1. Human CMV is a common opportunistic virus that establishes lifelong latency following primary infection. Transplant recipients with latent CMV infection are susceptible to viral reactivation, which can cause significant symptomatic and/or tissue-invasive disease leading to end-organ damage (collectively termed as "CMV disease"). This in turn increases the risk of graft dysfunction, graft failure, and mortality.

2.2. The Committee heard that in Singapore, there are over 270 adult solid organ transplant and haematopoietic stem cell transplant recipients treated in PHIs annually. Of these, approximately 30 patients are estimated to develop refractory or drug-intolerant CMV infection/disease each year.

2.3. For patients with refractory or drug-intolerant CMV infection/disease, treatment selection is individualised based on response to prior antiviral therapy and toxicity profile. Standard treatment options include ganciclovir or valganciclovir ("(val)ganciclovir"), which are included on the Standard Drug List, as well as foscarnet or cidofovir. However, most available therapies require intravenous administration, and their use may be associated with adverse effects that warrant consideration in transplant recipients, including myelosuppression with (val)ganciclovir and nephrotoxicity with foscarnet and cidofovir.

2.4. Consistent with clinical practice guidelines, maribavir would be expected to be used as a treatment option for refractory or drug-intolerant CMV infection/disease, subject to funding. This reflects its oral route of administration and capacity for use in the outpatient setting, with a different safety profile compared with currently available therapies. The Committee acknowledged the clinical need for additional treatment options in this setting and considered that listing maribavir may improve access and support appropriate patient care.

## Clinical effectiveness and safety

3.1. The Committee reviewed the published clinical evidence from the pivotal phase III, open-label, randomised controlled trial (SOLSTICE) in adults with post-transplant CMV infection/disease refractory, with or without genotypic resistance, to the most recently administered antiviral treatment. SOLSTICE compared maribavir with investigator-assigned treatment (IAT), comprising (val)ganciclovir, foscarnet, cidofovir, or combination therapy with foscarnet plus (val)ganciclovir. While the trial did not enrol patients based on intolerance to prior therapy, the Committee noted the unmet need for these patients and considered the evidence applicable to this group, consistent with the scope of the HSA-approved label.

3.2. The Committee noted that SOLSTICE met both its primary endpoint of CMV viraemia clearance at week 8, and its key secondary endpoint of CMV viraemia clearance with symptom control at week 8, maintained through week 16. Patients who received maribavir had significantly higher response rates than those in the IAT group for the primary endpoint (55.7% versus 23.9%, $p<0.001$) and the secondary endpoint (18.7% versus 10.3%, $p=0.01$). However, 26% of patients in the maribavir arm developed treatment-emergent resistance to maribavir, which attenuated the response rates over time.

3.3. While limitations in the design and conduct of the open-label trial may have introduced biases in favour of maribavir, the Committee considered that the consistent direction of effects across the primary and key secondary outcomes supports a clinical claim of superiority over the current standard of care, as represented by IAT in SOLSTICE.

3.4. In terms of safety, the Committee heard that maribavir was generally well-tolerated. Compared with IAT, maribavir was associated with a higher incidence of treatment-emergent adverse events (TEAEs) (97.4% versus 91.4%). These were mainly due to dysgeusia, which was mostly mild in severity. The trial also reported lower rates of neutropenia (9.4% versus 22.4%), hypokalaemia (3.4% versus 9.5%), and discontinuation due to TEAEs (13.2% versus 31.9%) for maribavir compared with IAT. Overall, the Committee considered maribavir to have a different but non-inferior safety profile to standard of care.

## Cost effectiveness

4.1. The Committee reviewed the economic evaluations published by overseas HTA agencies, which reported acceptable incremental cost-effectiveness ratios when comparing maribavir with IAT in adult transplant recipients with refractory or drug-intolerant CMV infection/disease. They also noted that maribavir is reimbursed in most overseas reference jurisdictions.

4.2. The Committee heard that the company's proposed price for maribavir was comparable to that in overseas reference jurisdictions. Overall, they considered that maribavir represented an acceptable use of healthcare resources in Singapore for treating post-transplant CMV infection/disease in adults who are refractory or intolerant to prior antiviral therapy.

## Estimated annual technology cost

5.1. The Committee noted that the cost impact to the public healthcare system was estimated to be less than SG$1 million per year in the first five years of listing maribavir on the MOH List of Subsidised Drugs.

## Recommendations

6.1. Given the high clinical need, acceptable clinical evidence, and that maribavir is considered an acceptable use of healthcare resources, the Committee recommended listing maribavir 200 mg tablet on the Medication Assistance Fund (MAF) for treating post-transplant CMV infection or disease in adults who are refractory (with or without genotypic resistance) or intolerant to prior antiviral therapy.

6.2. The Committee also recommended maribavir to be used in line with additional clinical criteria (listed in the Annex) to govern its appropriate use in local practice. The criteria were developed in consultation with local clinical experts and are consistent with overseas reimbursement criteria.

## ANNEX

**MAF clinical criteria for maribavir for treating post-transplant CMV infection/disease in adults who are refractory (with or without genotypic resistance) or intolerant to prior antiviral therapy**

Treatment of adults with post-transplant cytomegalovirus (CMV) infection/disease, who meet at least one of the following criteria:

- No change or increase in CMV viral load after at least 2 weeks of prior antiviral treatment(s); or
- Confirmed CMV genetic mutation(s) associated with resistance to prior antiviral treatment(s); or
- Contraindicated or intolerant to prior antiviral treatment(s), including patients with severe myelosuppression or impaired renal function.

Treatment with maribavir should be initiated by, or in consultation with, a specialist physician with experience in transplant medicine, transplant infectious disease, or infectious diseases.

Treatment with maribavir should be discontinued if:

- There is no change or an increase in CMV viral load after at least 2 weeks of maribavir treatment; or
- Patient has confirmed CMV genetic mutation(s) associated with resistance to maribavir.