Technology Guidance

Selexipag

for treating pulmonary arterial hypertension

Technology Guidance from the MOH Drug Advisory Committee

Guidance Recommendations

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

- ✓ Selexipag 200 mcg, 400 mcg, 600 mcg and 800 mcg tablet, to be added as the second or third drug in a combination treatment for pulmonary arterial hypertension, in line with the following criteria:
  - Patient is already receiving an endothelin receptor antagonist and/or a phosphodiesterase type 5 inhibitor at maximum tolerated doses; and
  - Prior to adding selexipag treatment, patient is assessed to have intermediate to high risk of 1-year mortality (according to the European Society of Cardiology/European Respiratory Society risk-stratification tool) during follow-up.

Funding status

Selexipag 200 mcg, 400 mcg, 600 mcg and 800 mcg tablets are recommended for inclusion on the Medication Assistance Fund (MAF) for the abovementioned indication from 1 November 2025.

Higher-strength tablets of selexipag (1,000 mcg, 1,200 mcg, 1,400 mcg and 1,600 mcg) have not been recommended for inclusion on the MAF as they are currently not marketed in Singapore.

Updated: 16 September 2025

Factors considered to inform the recommendations for funding

Technology evaluation

1.1. At the July 2024 meeting, the MOH Drug Advisory Committee ("the Committee") considered the evidence presented for the technology evaluation of selexipag for treating pulmonary arterial hypertension (PAH). The Agency for Care Effectiveness (ACE) conducted the evaluation in consultation with clinical experts from public healthcare institutions and patient experts from local patient and voluntary organisations. Clinical and economic evidence for selexipag 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. PAH is a progressive disease that can cause right ventricular failure and premature death if untreated. The severity of PAH and the level of urgency for treatment were conventionally described using the World Health Organization functional classification (WHO-FC I to IV). However, recent international clinical practice guidelines recommend categorising patients into risk groups (e.g. low, intermediate, and high) using multiparametric risk-assessment tools that take WHO-FC, 6-minute walking distance, and other available data into account.

2.2. The Committee heard that PAH is managed with a combination of drugs that target different treatment pathways, and local clinical practice is in line with international guidelines.

2.3. The Committee noted that selexipag is an orally administered prostacyclin receptor agonist. They also noted that there is a clinical need, in certain groups of patients with PAH, for selexipag as an add-on therapy to reduce the risk of clinical worsening. For patients with an intermediate-low risk status while receiving an endothelin receptor antagonist (ERA) and/or a phosphodiesterase type 5 (PDE-5) inhibitor, selexipag add-on therapy may be considered. For patients with an intermediate-high or high risk

status despite receiving an ERA and/or PDE-5 inhibitor, selexipag add-on therapy may be considered if adding an intravenous prostacyclin analogue (epoprostenol) was not feasible.

2.4. The Committee considered 17 testimonials from local patient experts and their carers about living with pulmonary hypertension. They heard that pulmonary hypertension had significantly impacted patients' physical, mental and emotional well-being, and had added burden to the patients' families. The Committee noted that patients experienced symptoms such as fatigue, breathlessness, rapid heart rate, and swelling in the legs and abdomen, which hindered simple daily activities, and impacted their social life and ability to work. The Committee noted that respondents had received different combinations of treatments, including ambrisentan, digoxin, epoprostenol, macitentan, ralinepag, riociguat, sildenafil, treprostinil and warfarin. Respondents reported generally feeling better, with less breathlessness, while on treatment.

2.5. The Committee acknowledged that five patient experts had received selexipag and had experienced variable outcomes, with one patient indicating they had reduced breathlessness, while another had still experienced a rapid heart rate despite being on treatment. The Committee noted that most patient experts were willing to accept manageable side effects of a new treatment if it could slow disease progression and improve symptoms. Overall, the respondents welcomed new treatment options for pulmonary hypertension that could improve quality of life, reduce symptoms, slow disease progression and, most importantly, be more affordable.

Clinical effectiveness and safety

3.1. The Committee reviewed the clinical evidence from a randomised controlled trial (GRIPHON) that compared selexipag with placebo in patients with PAH. At baseline, about 98% of patients had WHO-FC II or III symptoms. For the majority of patients (80%) who were already receiving stable doses of an ERA and/or PDE-5 inhibitor, selexipag and placebo were given as add-on therapies.

3.2. The primary efficacy endpoint of GRIPHON was a composite of all-cause death or a PAH-related complication (including disease progression or worsening of PAH that resulted in hospitalisation, and initiation of parenteral prostanoid therapy or long-term oxygen therapy, etc) up to the end of the treatment period.

3.3. The results showed that the risk of the primary composite endpoint was significantly lower with selexipag than with placebo (hazard ratio 0.60; 99% confidence interval 0.46 to 0.78; $p<0.001$). However, the treatment effect was driven by differences in disease progression and hospitalisation, and there was no significant difference in mortality between the two study groups. In subgroup analyses, the effect of selexipag was generally consistent across patient subgroups with different baseline PAH therapies, WHO FCs, and PAH aetiologies.

3.4. In the trial, more patients in the selexipag group discontinued their assigned treatment due to adverse events (AEs) compared with the placebo group. The most common AEs reported with selexipag were headache, diarrhoea, nausea and jaw pain, which were consistent with the known side effects of prostacyclin therapies.

3.5. Overall, the Committee considered that for treating patients with PAH, selexipag add-on therapy was superior to placebo in clinical effectiveness but inferior to placebo in safety.

Cost effectiveness

4.1. The company of selexipag was invited to submit a pricing proposal for their product for funding consideration. The Committee noted that the company was marketing lower-strength tablets of selexipag (200 to 800 mcg), but not higher-strength tablets (1,000 to 1,600 mcg). The Committee also noted that approximately 25% of selexipag-treated patients may require higher doses of ≥1,000 mcg based on local published literature. As these patients have to take two lower-strength tablets per dose, this would increase treatment costs and reduce affordability, based on the tablet prices proposed by the company. Overall, the Committee considered that the unavailability of higher-strength tablets would likely impact the cost effectiveness of selexipag treatment in Singapore.

4.2. The Committee reviewed a cost-effectiveness analysis conducted by ACE using data from the GRIPHON trial that compared selexipag with placebo in patients with PAH. At the prices proposed by the company, selexipag had a high base-case incremental cost-effectiveness ratio (ICER) between SG$245,000 and SG$285,000 per quality-adjusted life year (QALY) gained compared with placebo.

4.3. When the model parameters were varied across the range of possible values in sensitivity and scenario analyses, the ICERs for selexipag remained unacceptably high (ranging between SG$165,000 and more than SG$365,000 per QALY gained). The Committee noted the key drivers of the model were the cost of selexipag, the proportion of patients requiring higher selexipag doses, and the rate of PAH-related hospitalisation for patients in the FC IV health state.

4.4. Based on the analyses, the Committee considered that selexipag did not represent a cost-effective use of healthcare resources for treating PAH at the prices proposed by the company.

Estimated annual technology cost

5.1 The Committee noted the estimated cost impact to the public healthcare system was between SG$3 million and SG$5 million in the first year of listing selexipag on the MOH List of Subsidised Drugs for treating PAH. They acknowledged that the cost impact in subsequent years was uncertain and might increase substantially given the size of the PAH population and the progressive nature of the disease.

Recommendations (July 2024)

6.1. Based on available evidence, the Committee recommended not listing selexipag on the MOH List of Subsidised Drugs as an add-on therapy for patients with PAH who are insufficiently controlled with an ERA and/or PDE-5 inhibitor. The decision was based on the unfavourable cost effectiveness of selexipag compared with placebo at the prices proposed by the company.

Updated recommendations (June 2025)

7.1. Following a negative recommendation by the Committee at the July 2024 meeting, the company of selexipag submitted a revised pricing proposal for funding consideration.

7.2. The Committee noted that the higher-strength tablets of selexipag (1,000 to 1,600 mcg) would remain unavailable in Singapore. Nonetheless, the company's revised pricing proposal was adequate to improve the overall cost effectiveness of selexipag compared with placebo and manage the uncertainty of the budget impact.

7.3. Therefore, the Committee recommended selexipag 200 mcg, 400 mcg, 600 mcg and 800 mcg tablets be listed on the Medication Assistance Fund (MAF) as an add-on therapy for patients with PAH who are already receiving an ERA and/or a PDE-5 inhibitor at maximum tolerated doses. Prior to adding selexipag treatment, patients must be assessed to have intermediate to high risk of 1-year mortality (according to the European Society of Cardiology/European Respiratory Society risk-stratification tool) during follow-up.

VERSION HISTORY

Guidance on selexipag for treating pulmonary arterial hypertension

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 13 Sep 2024

2. **Guidance updated to include selexipag on the Medication Assistance Fund**

   Date of Publication 16 Sep 2025

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.

This 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.

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

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