

Rivastigmine

for the treatment of dementia associated with Alzheimer's disease or Parkinson's disease

Technology Guidance from the MOH Drug Advisory Committee

Guidance Recommendations

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

- ✓ Rivastigmine patch formulation (4.6mg/24h and 9.5mg/24h) for the treatment of moderately severe dementia, and behavioural symptoms of dementia, associated with Parkinson's disease.
- ✓ Rivastigmine patch formulation (4.6mg/24h, 9.5mg/24h and 13.3mg/24h) for the treatment of moderately severe dementia, and behavioural symptoms of dementia, associated with Alzheimer's disease.

Conditions should be confirmed by a specialist physician (geriatrician, neurologist or psychiatrist) with experience in the treatment of dementia.

Treatment should be continued only when it is considered to be having a worthwhile effect on cognitive, global, functional or behavioural symptoms.

Subsidy status

Rivastigmine patch formulation (4.6mg/24h, 9.5mg/24h and 13.3mg/24h) is recommended for inclusion on the Medication Assistance Fund (MAF) for the abovementioned indications.

Rivastigmine should be used in line with the clinical criteria in the MAF checklist for initial and continuing prescriptions. Treatment effect has to be re-assessed 6-monthly before further MAF assistance is granted for additional prescriptions.

MAF assistance **does not** apply to rivastigmine capsules (1.5mg, 3mg, 4.5mg and 6mg).

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 rivastigmine capsule and patch formulations for the treatment of dementia associated with Alzheimer's disease (AD) and Parkinson's disease (PD). The Agency for Care Effectiveness conducted the evaluation in consultation with clinical experts from the public healthcare institutions. Published clinical and economic evidence for rivastigmine was considered in line with its registered indications.
- 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
 - 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 Acetylcholinesterase inhibitors (AChEIs such as donepezil and rivastigmine) constitute routine clinical practice in Singapore for the management of patients with dementia due to AD or PD.
- 2.2 The Committee noted that rivastigmine is the only drug for dementia available in a transdermal (patch) formulation, and is the only drug approved by HSA for the treatment of dementia associated with PD in Singapore.
- 2.3 The Committee considered that there was limited clinical need to support listing rivastigmine oral capsules on SDL or MAF as patients were already able to receive donepezil (film-coated tablet) through SDL, or MAF (oral dispersible tablet) as a cheaper alternative treatment option.

Clinical effectiveness and safety

- 3.1 The Committee noted that the available clinical evidence suggested that rivastigmine was clinically comparable to donepezil in terms of efficacy (cognition, global outcomes and behavioural outcomes) and risk of adverse events in patients with mild to moderately severe AD. It acknowledged that limited data existed for the use of rivastigmine patch in severe AD compared with donepezil.
- 3.2 The Committee recognised from the literature that rivastigmine capsules led to small improvements in cognition, and to a lesser extent, functional and global outcomes, compared with placebo, in patients with PD. The small magnitude of these benefits was considered comparable to those observed among patients with AD who were treated with other AChEIs. The frequency of cholinergic adverse effects was considered moderate compared with placebo, and was noted to be further reduced with the use of the patch formulation.

Cost effectiveness

- 4.1 The Committee acknowledged the previous economic evaluation of AChEIs for AD conducted in 2013, and noted that the cost of rivastigmine used in the analysis was consistent with current prices. It noted however, that donepezil is likely to be more cost effective now following price decreases and the availability of generic formulations since the evaluation was conducted.
- 4.2 Value-based pricing negotiations were conducted with the manufacturer of rivastigmine, however, despite the price discount offered, the cost price of rivastigmine (both capsule and patch formulations) remained considerably higher than the cost of patented donepezil.
- 4.3 Limited economic evidence was available supporting the use of rivastigmine in PD. The Committee considered that results from overseas cost effectiveness studies were unlikely to be generalisable to the local context, but agreed that the price proposed by the manufacturer was acceptable if its use was limited to patients with moderately severe disease and those who could demonstrate continued meaningful response to treatment.

Additional considerations

- 5.1 Despite the limited clinical and economic evidence to support the use of rivastigmine patch in AD and PD, the Committee noted a therapeutic gap in the transdermal treatment of dementia. It considered that the patch formulation was associated with greater ease of use and monitoring, which made it the preferred treatment option by caregivers, and noted that treatment adherence might be improved with the use of transdermal drug delivery. Furthermore, they acknowledged clinical expert testimony that the use of the patch formulation was important in relieving caregiver burden, particularly for patients with behavioural symptoms associated with moderately severe dementia. In addition, rivastigmine patch was noted to be the preferred formulation for patients with PD, many of whom develop swallowing impairment during the course of their disease.
- 5.2 The Committee highlighted that clinical criteria were needed to govern appropriate treatment cessation when rivastigmine was no longer producing an effect. The Committee therefore recommended that the listing of rivastigmine patch on MAF should be accompanied by a clinical checklist to ensure that clinical outcomes for each patient are re-assessed every 6 months before further financial assistance is granted for additional prescriptions.

Estimated annual technology cost

- 6.1 The Committee estimated that around 200 people with moderately severe dementia associated with AD or PD in Singapore would benefit from government assistance for rivastigmine patch. The annual cost impact was estimated to be less than \$500,000 in the first year of listing on the MAF at the price proposed by the manufacturer.

Recommendation

- 7.1 The Committee recommended rivastigmine patch formulation for listing on the MAF for the treatment of moderately severe dementia, and behavioural symptoms of dementia, associated with Alzheimer’s disease or Parkinson’s disease, on the basis of high clinical need in the absence of alternative transdermal treatment options.
- 7.2 Initiation and continuation of treatment with rivastigmine patch should be governed by specific clinical criteria outlined in an MAF checklist.
- 7.3 Rivastigmine capsules were not recommended for listing on MAF due to a lack of clinical need, and in light of their higher cost prices compared with oral donepezil which were not justified by the benefits they offered.

About the Agency

The Agency for Care Effectiveness (ACE) is the national health technology assessment agency in Singapore residing within the Ministry of Health. It conducts evaluations to inform the subsidy of treatments, and produces guidance on the appropriate use of treatments for public hospitals and institutions in Singapore. When using the guidance, the responsibility for making decisions appropriate to the circumstances of the individual patient remains with the healthcare professional.

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