Technology Guidance

Dexamethasone intravitreal implant

for treating diabetic macular oedema, retinal vein occlusion and non-infectious uveitis

Technology Guidance from the MOH Drug Advisory Committee

Guidance Recommendations

The Ministry of Health's Drug Advisory Committee has not recommended listing dexamethasone 0.7 mg intravitreal implant on the MOH List of Subsidised Drugs for treating diabetic macular oedema, macular oedema following retinal vein occlusion and non-infectious uveitis affecting the posterior segment of the eye. The decision was based on the unfavourable clinical and cost-effectiveness of intravitreal dexamethasone implant compared with current treatment options.

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Factors considered to inform the recommendations for funding

Technology evaluation

1.1. At the June 2023 meeting, the MOH Drug Advisory Committee ("the Committee") considered the evidence presented for the technology evaluation of dexamethasone intravitreal implant for treating diabetic macular oedema (DMO), macular oedema following branch retinal vein occlusion (BRVO) or central retinal vein occlusion (CRVO) and non-infectious uveitis (NIU) affecting the posterior segment of the eye. The Agency for Care Effectiveness (ACE) conducted the evaluation in consultation with clinical experts from public healthcare institutions (PHIs). Local patient and voluntary organisations were also invited to provide their lived experiences to inform the evaluation, however, no submissions were received. Published clinical and economic evidence for dexamethasone implant 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; 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. In local clinical practice, intravitreal anti-vascular endothelial growth factor (anti-VEGF) injections represent the preferred treatment option for DMO and macular oedema following retinal vein occlusion (RVO). Dexamethasone implant may be considered as an alternative to another anti-VEGF treatment in patients who have had an inadequate response to prior anti-VEGF treatment. For a minority of patients who are deemed unsuitable for anti-VEGF, such as those with recent cardiovascular events, initial treatment with dexamethasone implant may also be considered.

2.2. Currently subsidised anti-VEGF treatments for DMO and RVO include ranibizumab and bevacizumab. The Committed noted that other anti-VEGF treatments (faricimab and aflibercept) were also being considered at the same meeting.

2.3. For NIU affecting the posterior segment of the eye, the treatment options used locally

are intravitreal dexamethasone implant as well as unregistered or off-label use of periocular or intravitreal triamcinolone.

Clinical effectiveness and safety

Diabetic macular oedema and macular oedema following retinal vein occlusion

Dexamethasone implant versus anti-VEGF

3.1. The Committee reviewed the clinical evidence from various head-to-head randomised controlled trials (RCTs) and considered dexamethasone implant to be inferior in efficacy compared with ranibizumab. The Committee acknowledged there were potential differences between the population of interest and trial populations with respect to prior failed anti-VEGF treatment.

3.2. In Trial 024 involving patients with DMO, dexamethasone implant resulted in a significantly lower proportion of patients who achieved best corrected visual acuity (BCVA) improvement of at least 15 Early Treatment Diabetic Retinopathy Study (ETDRS) letters from baseline and a lower mean BCVA improvement from baseline compared with ranibizumab. Similarly, dexamethasone implant resulted in a significantly lower proportion of patients who achieved BCVA improvement of at least 15 ETDRS letters and lower mean BCVA improvement among patients with BRVO (COMO, COMRADE-B) and CRVO (COMRADE-C).

3.3. Overall, considering the established clinical comparability of anti-VEGF treatments (ranibizumab, faricimab and aflibercept) for treating DMO and RVO, the Committee concluded that dexamethasone implant was less effective than anti-VEGF treatments.

Dexamethasone implant versus sham

3.4. The Committee reviewed the clinical evidence from two identically-designed, double-blind, phase III RCTs (MEAD trials) comparing dexamethasone implant with sham in patients with DMO. The Committee agreed dexamethasone implant was superior to sham in terms of efficacy, especially for pseudophakic eyes, in which a more consistent treatment effect was observed over time.

3.5. For patients with RVO, the Committee agreed that dexamethasone implant was superior to sham in efficacy, based on evidence from three RCTs (GENEVA 008, GENEVA 009 and Trial 020). Notably, dexamethasone implant resulted in a significantly higher proportion of patients who achieved BCVA improvement of at least 15 ETDRS letters from baseline compared with sham at days 60 and 90, but not at 6 months. The Committee noted the waning of treatment effect before 6 months which could be mitigated by an increased dosing frequency (instead of 6-monthly), as practised in local clinical setting.

3.6. In terms of safety, the Committee agreed that dexamethasone implant was inferior to anti-VEGF or sham. For DMO, higher incidence of cataracts and elevated intra-ocular

pressure were observed with dexamethasone implant compared with anti-VEGF and sham. There were also more cases of ocular hypertension and conjunctival haemorrhage with dexamethasone implant across RVO trials.

Non-infectious uveitis

3.7. The Committee considered that the available data provided limited comparative information. Based on an open-label phase III RCT (POINT), there was no significant difference between dexamethasone implant and intravitreal triamcinolone in mean BCVA improvement from baseline at week 8. While dexamethasone implant resulted in a statistically larger mean improvement in visual acuity at week 8 compared with periocular triamcinolone, this difference was less than the minimal clinically important difference (MCID) of 10 to 15 ETDRS letters. Overall, the Committee agreed that dexamethasone implant was likely comparable in efficacy to triamcinolone in the short term.

3.8. In terms of safety, the Committee considered dexamethasone implant inferior to triamcinolone as there were more cases of increased intraocular pressure of at least 10 mmHg from baseline and elevated intraocular pressure of at least 24 mmHg with dexamethasone implant.

Cost effectiveness

4.1. The company of dexamethasone implant was invited to submit a value-based pricing proposal for their product for funding consideration in line with the HSA-approved indications.

4.2. The Committee considered the uncertainty around the cost-effectiveness of dexamethasone implant was not adequately addressed by the proposal given its cost in relation to anti-VEGF treatments and inferior efficacy and safety. The Committee also noted the substantially higher treatment cost of dexamethasone implant versus triamcinolone. Overall, the Committee considered dexamethasone implant was not likely to represent a cost-effective use of healthcare resources.

Estimated annual technology cost

5.1. The Committee noted that the annual cost impact to the public healthcare system was estimated to be less than SG$1 million in the first year of listing dexamethasone intravitreal implant on the MOH List of Subsidised Drugs for treating DMO, RVO and NIU.

Recommendations

6.1. Based on available evidence, the Committee recommended not listing dexamethasone intravitreal implant on the MOH List of Subsidised Drugs for treating DMO, RVO and NIU in view of unfavourable clinical and cost-effectiveness compared with current treatment options.

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.

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