[GUIDANCE IS OUTDATED AND HAS BEEN WITHDRAWN ON 6 FEBRUARY 2026.]

Omalizumab

for treating antihistamine-resistant chronic spontaneous urticaria

Technology Guidance from the MOH Drug Advisory Committee

Guidance Recommendations

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

- ✓ Omalizumab 150 mg powder and solvent for solution for injection as an add-on therapy to H_1-antihistamines for treating severe chronic spontaneous urticaria (CSU) in patients aged 12 years and older, with a mean weekly Urticaria Activity Score (UAS7) of 28 and above, despite the use of, or who are intolerant to, four-times registered dose of second-generation non-sedating H_1-antihistamines.

A maximum of six 300 mg doses of omalizumab should be administered for each treatment course. Re-treatment with omalizumab can be considered upon relapse for patients who achieve an adequate response during the previous treatment course.

Adequate response to omalizumab is defined as a UAS7 score of six or below while on treatment.

Omalizumab should be prescribed by a specialist physician (immunologist, allergist, or dermatologist) with experience in managing CSU.

Subsidy status

Omalizumab 150 mg powder and solvent for solution for injection is recommended for inclusion on the Medication Assistance Fund (MAF) for the abovementioned indication.

Omalizumab should be used in line with the clinical criteria in the MAF checklist for initial and continuing prescriptions.

WITHDRAWN

Published on 2 January 2019

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 omalizumab for treating antihistamine-resistant CSU. The Agency for Care Effectiveness conducted the evaluation in consultation with the MOH Urticaria Expert Working Group comprising senior healthcare professionals from public healthcare institutions. Published clinical and economic evidence for omalizumab was considered in line with the 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 subsidy considerations.

Clinical need

2.1 The Committee noted that local practice was typically aligned with international clinical practice guidelines for treating CSU, where omalizumab and ciclosporin are used as add-on therapy for patients whose condition is unresponsive to four-fold registered dose of second-generation antihistamines.

2.2 The Committee also acknowledged that the 2017 revision of the EAACI/GA^{2}LEN/EDF/WAO guidelines suggested omalizumab should be used before ciclosporin because of its more favourable adverse effect profile.

2.3 The Committee noted ciclosporin was used off-label for CSU in Singapore and that neither ciclosporin nor omalizumab were subsidised for CSU at the time of the evaluation.

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Clinical effectiveness and safety

3.1 The Committee agreed that ciclosporin was the appropriate comparator for omalizumab for people with antihistamine-resistant CSU.

3.2 The Committee heard that no head-to-head trials directly compared omalizumab and ciclosporin for this indication. Thus, published placebo-controlled trials of omalizumab and ciclosporin were used to inform an indirect comparison between the two drugs.

3.3 Pairwise meta-analysis of omalizumab trials confirmed the treatment effect was dose-dependent. Omalizumab 300mg every four weeks was statistically significantly better than placebo across all outcomes at week 12 and clinically significant for mean change in Dermatology Quality of Life (DLQI) score at week 12. The 150 mg dose was statistically significantly better than placebo for all efficacy outcomes, but results were not clinically significant.

3.4 The Committee acknowledged that symptom control deteriorated after discontinuation of omalizumab, and reached the same level as the placebo arm within 12 to 16 weeks. They referred to the OPTIMA trial results which showed that a proportion (about 25%) of previous responders may not subsequently achieve adequate response (UAS7≤6) upon first retreatment with omalizumab. They also acknowledged that no clinical evidence was available to inform the rate of treatment waning in patients who stop and restart multiple rounds of treatment. Based on available evidence, the Committee agreed that retreatment with omalizumab was likely to be necessary for most patients after an initial treatment course, and clinical governance should be in place to allow continued use only in patients who are likely to benefit from retreatment.

3.5 Based on available short-term studies, the Committee considered omalizumab was well-tolerated, with a good safety profile. Incidence of headache, arthralgia, and administration site reaction were numerically higher in the omalizumab arm compared with placebo.

3.6 The Committee noted there was limited evidence from two small placebo-controlled RCTs to inform the clinical effectiveness of ciclosporin for CSU. Results showed the mean change in UAS7 score was statistically better in the ciclosporin group compared with placebo at week 4. However, the Committee acknowledged the result had a wide 95% confidence interval that did not lie completely beyond the minimal clinically important difference (MCID) estimate, therefore results were uncertain with regards to clinical significance.

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3.7 Results from the indirect comparison showed no statistical difference between omalizumab and ciclosporin with respect to mean change from baseline UAS7 score. However, the Committee agreed results should be interpreted with caution considering the differences in trial designs and patient characteristics between both drugs. The Committee also noted the lack of long-term safety data for omalizumab and agreed that the short-term safety profile of omalizumab was more favourable than ciclosporin.

3.8 Based on available evidence and the use of ciclosporin and omalizumab as add-on therapy at the same line of treatment in clinical practice for CSU, the Committee accepted the results from the indirect comparison to inform clinical comparability of both drugs among patients with an inadequate response to H_1-antihistamine treatment at up to four-fold H_1-antihistamine doses. The Committee noted that this conclusion was consistent with findings from HTA agencies in other jurisdictions such as Australia (PBAC), which have previously assessed omalizumab.

Cost effectiveness

4.1 ***Cost-minimisation for omalizumab versus ciclosporin***

The Committee acknowledged that the manufacturer of omalizumab offered a price discount, contingent upon an MAF listing at the same line or before ciclosporin as part of their value-based pricing (VBP) proposal. Results of a cost-minimisation analysis comparing omalizumab and ciclosporin showed omalizumab was cheaper than branded ciclosporin, but more expensive than generic ciclosporin over a six-month treatment period.

4.2 ***Cost-effectiveness of omalizumab versus placebo***

The Committee considered results from ACE's cost-effectiveness analysis which compared omalizumab with placebo after failure of H_1-antihistamine therapy. For patients with moderate-to-severe CSU, omalizumab was associated with a base-case incremental cost-effectiveness ratio (ICER) between SG$45,000 to <SG$75,000 per QALY gained compared with placebo. Results from sensitivity analyses were largely consistent with the base case estimates. Scenario analyses which restricted omalizumab to patients with severe CSU resulted in a more favourable ICER which fell within the range of SG$15,000 to <SG$45,000 per QALY gained.

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Estimated annual technology cost

5.1 The Committee estimated around 34 people with severe CSU in Singapore would benefit from government assistance for omalizumab. The annual cost impact was estimated to be less than SG$500,000 in the first year of listing on the MAF.

Additional considerations

6.1 The Committee noted that given its limited evidence, off-label use of ciclosporin has not been recommended for subsidy for treating CSU in overseas countries such as Australia (PBAC), UK (NICE), New Zealand (PHARMAC), or Canada (CADTH). Furthermore, the Committee noted that the majority of public healthcare institutions currently stock branded ciclosporin for use in organ transplantation, and including generic ciclosporin in their inventories could potentially lead to dispensing errors.

Recommendation

7.1 Based on available evidence, the Committee recommended omalizumab 150 mg powder and solvent for solution for injection be listed on the MAF for treating antihistamine-resistant chronic spontaneous urticaria in line with specific clinical criteria, given its favourable clinical and cost-effectiveness and the clinical need for subsidised treatment to ensure appropriate patient care.

WITHDRAWN

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.

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

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