

[GUIDANCE IS OUTDATED AND HAS BEEN WITHDRAWN ON 1 JULY 2022. PLEASE REFER TO GUIDANCE ON TOFACITINIB, USTEKINUMAB AND VEDOLIZUMAB FOR TREATING INFLAMMATORY BOWEL DISEASE FOR UP TO DATE SUBSIDY INFORMATION ON THIS TOPIC].

Vedolizumab

for treating ulcerative colitis and Crohn's disease

Technology Guidance from the MOH Drug Advisory Committee

Guidance Recommendations

The Ministry of Health's Drug Advisory Committee has not recommended listing vedolizumab on the Medication Assistance Fund (MAF) for treating ulcerative colitis and Crohn's disease because of unacceptable cost-effectiveness compared with biosimilar infliximab at the price proposed by the manufacturer.

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Factors considered to inform the recommendations for subsidy

Technology evaluation

- 1.1 The MOH Drug Advisory Committee (“the Committee”) considered the evidence presented for vedolizumab for treating ulcerative colitis and Crohn’s disease. The Agency for Care Effectiveness conducted the evaluation in consultation with clinical experts from the public healthcare institutions. Published clinical and economic evidence for vedolizumab 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 subsidy considerations.

Clinical need

- 2.1 Vedolizumab is a monoclonal antibody that blocks $\alpha4\beta7$ integrin in the gut to reduce chronic intestinal inflammation. The Committee noted that vedolizumab is used as first-line biologic therapy after failure of conventional agents (same place in therapy as TNF-alpha inhibitors) or second-line biologic therapy in those who have an inadequate response to TNF-alpha inhibitors, in line with international clinical guidelines for the management of ulcerative colitis and Crohn’s disease.
- 2.2 The Committee acknowledged that biosimilar infliximab, adalimumab, and golimumab are currently listed on the Medication Assistance Fund (MAF) for these conditions. Therefore, they considered that there was low clinical need for an additional subsidised biologic treatment for patients.

Clinical effectiveness and safety

- 3.1 The Committee considered the clinical evidence and acknowledged that no studies directly compared vedolizumab to infliximab (main comparator) or adalimumab for the treatment of ulcerative colitis or Crohn's disease. Indirect comparisons of vedolizumab against infliximab or adalimumab were limited by heterogeneity of the study designs and characteristics of patients among the placebo-controlled trials. The Committee also acknowledged the effectiveness of vedolizumab was lower in patients who had received prior treatment with an anti-TNF inhibitor compared to treatment-naïve patients.
- 3.2 For patients with ulcerative colitis, the Committee noted GEMINI I showed vedolizumab was statistically significantly more effective than placebo in achieving clinical response at week 6 (induction phase), and clinical remission at week 52, in a mixed trial population comprising treatment-naïve patients and patients with an inadequate response to TNF alpha inhibitors. For patients with Crohn's disease, the Committee noted that GEMINI II showed vedolizumab was not more effective than placebo in achieving clinical response at week 6 (primary endpoint) in a mixed trial population. However, vedolizumab was statistically significantly more effective than placebo in achieving clinical remission at week 6, and maintaining clinical response and clinical remission at week 52.
- 3.3 The Committee acknowledged that GEMINI III (comprising 76% of patients who had failed a TNF-alpha inhibitor) showed vedolizumab was not statistically significantly more effective than placebo in achieving remission at week 6 (primary endpoint) in patients who had failed prior TNF-alpha inhibitor treatment. However, results at week 10 showed vedolizumab was statistically significantly more effective than placebo in achieving clinical remission in patients who had failed a TNF-alpha inhibitor, and in the mixed trial population.
- 3.4 The Committee noted treatment adverse events were similar in the vedolizumab and placebo groups in the clinical trials for both indications, and no cases of progressive multifocal leukoencephalopathy were reported.
- 3.5 The Committee noted there was insufficient evidence to conclude any difference in comparative efficacy and safety between vedolizumab and infliximab or adalimumab for treating ulcerative colitis and Crohn's disease. However, it acknowledged an evaluation by the PBAC (Australia) considered that vedolizumab may be a reasonable alternative to infliximab despite high heterogeneity between the trials in the indirect comparison.

Cost effectiveness

- 4.1 The Committee considered the cost-effectiveness of vedolizumab based on published studies, acknowledging there were no local economic evaluations available. Based on available evidence, the Committee agreed a cost-minimisation approach was most appropriate to compare the cost of vedolizumab with biosimilar infliximab.
- 4.2 The Committee noted that at the price proposed by the manufacturer as part of value-based pricing (VBP) discussions, the annual cost of vedolizumab per patient was considerably higher than for biosimilar infliximab based on their equi-effective doses. Furthermore, the Committee noted that the annual cost of vedolizumab was likely to increase when dosed at 4-weekly intervals, for patients who have a suboptimal response to 8-weekly dosing. In view of the large cost difference between the agents, the Committee considered that vedolizumab was not cost-effective in Singapore compared to biosimilar infliximab at the price proposed by the manufacturer.

Estimated annual technology cost

- 5.1 The Committee noted that approximately 48 people with ulcerative colitis or Crohn's disease in Singapore would benefit from listing vedolizumab on the MAF. The annual cost impact was estimated to be between SG\$500,000 to <SG\$1 million in the first year of listing.

Recommendation

- 6.1 Based on available evidence, the Committee recommended not listing vedolizumab on the MAF in view of unfavourable cost-effectiveness given its high cost compared with biosimilar infliximab at the price proposed by the manufacturer.

HTA DRAFT

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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