Technology Guidance

[GUIDANCE IS OUTDATED AND HAS BEEN WITHDRAWN ON 31 AUGUST 2022.]

Guselkumab, ixekizumab and secukinumab

for treating chronic plaque psoriasis

Technology Guidance from the MOH Drug Advisory Committee

Guidance Recommendations

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

- ✓ Ixekizumab 80 mg/ml solution for injection prefilled pen for treating adults with chronic plaque psoriasis.

Subsidy status

Ixekizumab 80 mg/ml solution for injection prefilled pen is recommended for inclusion in the Medication Assistance Fund (MAF) for the abovementioned indication.

Ixekizumab should be used in line with the clinical criteria in the MAF checklist for initial and continuing prescriptions for patients with chronic plaque psoriasis.

MAF assistance **does not** apply to any formulations or strengths of guselkumab or secukinumab.

Published: 18 January 2021

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 interleukin inhibitors (guselkumab, ixekizumab and secukinumab) for treating adults with chronic plaque psoriasis. The manufacturer of ustekinumab, another interleukin inhibitor approved for treating plaque psoriasis, did not want their product evaluated for subsidy consideration. The Agency for Care Effectiveness conducted the evaluation in consultation with the MOH Psoriasis Expert Working Group comprising senior healthcare professionals from the public healthcare institutions. Published clinical and economic evidence for guselkumab, ixekizumab and secukinumab was considered in line with their 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 subsidy considerations.

Clinical need

2.1. The Committee acknowledged that in local practice, biologics are usually only used to treat chronic plaque psoriasis if patients meet specific severity criteria (Psoriasis Area Severity Index (PASI) >10, and Dermatology Life Quality Index (DLQI) >10) and have had an inadequate response to conventional therapies (topical treatment, phototherapy and oral therapy), unless contraindicated.

2.2. The Committee noted that approximately 10% of patients with moderate to severe chronic plaque psoriasis are likely to require treatment with a biologic. Local expert opinion confirmed that any biologic (e.g. anti-TNFα, IL-17 inhibitor, IL-12/23 inhibitor) may be considered as first-line biologic therapy, however, interleukin inhibitors are usually preferred over anti-TNFα biologics for patients with psoriasis alone, while anti-TNFα biologics are considered for patients who have concomitant psoriatic arthritis.

2.3. While anti-TNFα biologics (adalimumab biosimilar, infliximab biosimilar and etanercept) are already subsidised for this condition, the Committee agreed that there was a clinical need to improve the affordability of alternative biologic treatment options for patients.

Clinical effectiveness and safety

3.1. The Committee agreed that adalimumab, etanercept and infliximab were appropriate comparators to guselkumab, ixekizumab and secukinumab. The three interleukin inhibitors were also compared with each other.

3.2. The Committee reviewed available evidence from seven randomised controlled trials (RCTs) which compared guselkumab, ixekizumab or secukinumab with anti-TNFα biologics or each other for treating adults with moderate to severe chronic plaque psoriasis.

3.3. Interleukin inhibitors versus anti-TNFα biologics
The Committee heard that direct evidence showed that guselkumab, ixekizumab and secukinumab led to statistically significant improvements in PASI 75, 90 and 100 response rates, the proportion of patients who achieved a modified Investigator's Global Assessment (mIGA) or static Physician's Global Assessment (sPGA) score of 0/1 and the proportion of patients who achieved a DLQI score of 0/1 compared to anti-TNFα biologics (adalimumab and etanercept). Based on the available evidence, the Committee agreed that all three interleukin inhibitors were superior in efficacy to anti-TNFα biologics for treating chronic plaque psoriasis.

3.4. Interleukin inhibitors versus interleukin inhibitors
Head-to-head trials comparing ixekizumab with guselkumab (IXORA-R) and secukinumab with guselkumab (ECLIPSE) were identified. The Committee noted ixekizumab resulted in statistically significant improvements in PASI 100 responses and sPGA scores compared with guselkumab at week 12 in the IXORA-R trial. However, PASI 75 and PASI 90 results at week 12 were not published. The Committee considered that the week 12 results should be interpreted with caution as the response curves for the PASI and global assessment score endpoints showed that clinical response with guselkumab generally peaked around week 16 or later.

3.5. In the ECLIPSE trial, the Committee noted that guselkumab resulted in a statistically significant improvement in PASI 90 compared with secukinumab at week 48. However, guselkumab was non-inferior to secukinumab in the proportion of patients who achieved PASI 75 responses at weeks 12 and 48 (composite endpoint, non-significant result for superiority test).

3.6. The Committee acknowledged results of network meta-analyses considered by NICE (UK) which showed that all three interleukin inhibitors were comparable in efficacy based on PASI 75 response.

3.7. Taking into account direct evidence from the IXORA-R and ECLIPSE trials and indirect evidence from NICE, none of the interleukin inhibitors consistently showed superiority over one another for all PASI outcomes or timepoints measured. In the absence of consistent results, the Committee considered all interleukin inhibitors were comparable in efficacy.

3.8. Safety

The Committee agreed that all three interleukin inhibitors were generally well-tolerated in the trials. While the incidence of injection site reactions was numerically higher for ixekizumab than guselkumab, the Committee noted that these events were not serious adverse events and rarely led to treatment discontinuation. The Committee considered that the safety profile of all three interleukin inhibitors was comparable and was also similar to anti-TNFα biologics as a class.

Cost effectiveness

4.1. The Committee agreed that a cost-minimisation approach was appropriate to assess the cost-effectiveness of the interleukin inhibitors, in view of their comparable efficacy and safety.

4.2. The Committee acknowledged that the manufacturers of all three interleukin inhibitors offered price discounts, contingent upon an MAF listing, as part of their value-based pricing (VBP) proposals. Results of a cost-minimisation analysis showed that ixekizumab was the most cost-effective option. The proposed price was also lower than anti-TNFα biologics that were listed on the MAF at the time of evaluation.

Estimated annual technology cost

5.1. The Committee noted that the annual cost impact was estimated to be less than SG$1 million in the first year of listing ixekizumab on the MAF.

Recommendations

6.1. Based on available evidence, the Committee recommended ixekizumab 80 mg/ml solution for injection prefilled pen be listed on the MAF for treating adults with chronic plaque psoriasis in view of favourable clinical and cost effectiveness compared to anti-TNFα biologics at the price proposed by the manufacturer.

6.2. At the prices proposed by the manufacturers, guselkumab and secukinumab were not recommended for listing on the MAF due to unfavourable cost-effectiveness compared with ixekizumab.

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 subsidy decisions for treatments, diagnostic tests and vaccines, and produces guidance for public hospitals and institutions in Singapore.

This guidance is based on the evidence available to the MOH Drug Advisory Committee as at 19 August 2020. It 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

Principal Head (HTA)
Agency for Care Effectiveness
Email: ACE_HTA@moh.gov.sg