Technology Guidance

[GUIDANCE IS OUTDATED AND HAS BEEN WITHDRAWN ON 31 AUGUST 2022.]

Ixekizumab and secukinumab

for treating active psoriatic arthritis

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 active psoriatic arthritis.

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 active psoriatic arthritis.

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

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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 the technology evaluation of interleukin inhibitors (ixekizumab and secukinumab) for treating adults with active psoriatic arthritis. The manufacturer of ustekinumab, another interleukin inhibitor approved for treating psoriatic arthritis, did not want their product evaluated for subsidy consideration. The Agency for Care Effectiveness conducted the evaluation in consultation with the MOH Psoriatic Arthritis Expert Working Group comprising senior healthcare professionals from the public healthcare institutions. Published clinical and economic evidence for 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 biologics are only used to treat peripheral arthritis in local practice if patients have a minimum of three swollen and three tender joints/digits/entheses, and have had an inadequate response to two conventional synthetic disease-modifying antirheumatic drugs (csDMARDs; sulfasalazine, leflunomide, methotrexate or ciclosporin) that have each been administered for a minimum of three months, unless contraindicated.

2.2. In line with international clinical practice guidelines, patients with predominant axial disease may consider biologic treatment in local practice if they have failed to achieve an adequate response to two sequential non-steroidal anti-inflammatory drugs (NSAIDs) at maximal tolerated doses given for at least four weeks in total (two weeks each), unless contraindicated.

2.3. The Committee noted that approximately 30% of patients with psoriatic arthritis 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 or targeted synthetic DMARD) may be considered as first-line biologic therapy, in view of similar efficacy and safety across all drug classes. While anti-TNFα biologics (adalimumab biosimilar, infliximab biosimilar and golimumab) 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, golimumab and infliximab were appropriate comparators to ixekizumab and secukinumab. The two interleukin inhibitors were also compared with each other.

3.2. The Committee reviewed available evidence from eight randomised controlled trials (RCTs) which compared ixekizumab or secukinumab (150 mg or 300 mg dose) with placebo or anti-TNFα biologics for treating adults with active psoriatic arthritis. No head-to-head trials comparing the efficacy and safety of ixekizumab with secukinumab were identified. Results from the placebo-controlled trials showed that both ixekizumab and secukinumab were superior to placebo in the efficacy outcomes measured.

3.3. Interleukin inhibitors versus anti-TNFα biologics

In the open-label SPIRIT-H2H trial, use of ixekizumab resulted in a statistically significant improvement in the composite primary outcome of Psoriasis Area and Severity Index (PASI) 100 and American College of Rheumatology (ACR) 50 response compared with adalimumab at week 24. However, the Committee noted that this result was mainly driven by the PASI 100 endpoint. Ixekizumab was superior to adalimumab for PASI 75 and PASI 100 response rates but was non-inferior to adalimumab for the ACR 50 outcome alone. Also, no statistically significant differences were found between ixekizumab and adalimumab in terms of ACR 20 response rates.

3.4. In the double-blind EXCEED trial, no statistically significant difference in ACR 20 response rates between secukinumab (300 mg dose) and adalimumab at week 52 were reported. As the superiority of secukinumab versus adalimumab was not established for the primary endpoint (ACR 20), key secondary endpoints in the hierarchy were not formally tested for statistical significance. Secukinumab 150 mg dose was not studied in this trial.

3.5. Given that all three subsidised anti-TNFα biologics (adalimumab, golimumab, infliximab) were previously considered to be clinically comparable by the Committee in November 2016, results of the SPIRIT-H2H and EXCEED trials were extrapolated and the Committee agreed that ixekizumab and secukinumab were comparable in efficacy to anti-TNFα biologics as a class for treating active psoriatic arthritis based on the ACR outcome.

3.6. Interleukin inhibitors versus interleukin inhibitors

As there were no head-to-head trials comparing ixekizumab and secukinumab, an adjusted indirect comparison was conducted based on two placebo-controlled ixekizumab RCTs (SPIRIT-P1 and SPIRIT-P2) and four placebo-controlled secukinumab RCTs (FUTURE-2, 3, 4, 5), using placebo as a common reference arm, to determine the comparative efficacy of the two treatments.

3.7. The Committee heard that indirect results showed no significant differences between ixekizumab and secukinumab in terms of ACR 20 and ACR 50 response rates in the total population, which included a mix of patients who were naïve to anti-TNFα biologics (anti-TNFα-naïve) or had an inadequate response to, or were intolerant of anti-TNFα (anti-TNFα-IR). Subgroup analyses in anti-TNFα-naïve and anti-TNFα-IR patients also showed no significant differences between ixekizumab and secukinumab. PASI 75 response rates were also similar between the two biologics in the mixed population. The Committee agreed that ixekizumab and secukinumab were comparable in efficacy to each other for treating active psoriatic arthritis based on the ACR outcome and PASI 75 response.

3.8. Safety

The Committee agreed that both interventions were generally well-tolerated in the trials. In SPIRIT-H2H, adverse events were more common in the ixekizumab group compared with adalimumab, but discontinuations due to adverse events and serious adverse events were numerically higher in the adalimumab group. Incidence of adverse events for secukinumab was similar to that of adalimumab in EXCEED. While non-fatal serious adverse events occurred more frequently with secukinumab, discontinuations due to adverse events and injection-site reactions occurred more frequently with adalimumab. The Committee considered that the safety profile of the two interleukin inhibitors was comparable and was also similar to anti-TNFα biologics as a class.

3.9. The Committee acknowledged that results from ACE's evaluation were consistent with findings from other jurisdictions. PBAC (Australia) had previously considered ixekizumab to be non-inferior in terms of comparative effectiveness and safety to secukinumab, adalimumab and ustekinumab. Similarly, results of a network meta-analysis considered by NICE (UK) showed that secukinumab was similar to anti-TNFα biologics in improving joint symptoms in both biologic-naïve and experienced subpopulations. NICE also accepted that ixekizumab had comparable efficacy to secukinumab.

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 to anti-TNFα biologics and to each other.

4.2. The Committee acknowledged that the manufacturers of ixekizumab and secukinumab 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 more cost-effective than secukinumab (both 150 mg and 300 mg dosing regimens). 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 active psoriatic arthritis in view of favourable clinical and cost effectiveness compared to anti-TNFα biologics at the price proposed by the manufacturer and moderate clinical need for an alternative biologic treatment to be subsidised to ensure appropriate patient care.

6.2. At the price proposed by the manufacturer, secukinumab was 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

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