Infliximab

*for the treatment of rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, plaque psoriasis, 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 recommended:

- **✓** Infliximab biosimilar (Remsima) 100mg vial for the treatment of:
  - Adults with moderately to severely active rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, chronic plaque psoriasis, ulcerative colitis or Crohn’s disease
  - Children aged 6 to 17 years with severe active Crohn’s disease
  - Children aged 6 years or older with moderately to severely active ulcerative colitis

- **✓** The removal of infliximab reference biologic (Remicade) from the Medication Assistance Fund (MAF) for all indications, in view of its unacceptable cost-effectiveness at the price proposed by the manufacturer.

### Subsidy status

Infliximab biosimilar (Remsima) is recommended for inclusion on the MAF for the abovementioned conditions from 1 March 2018. MAF listing of Remicade will cease on 31 December 2018.

Remsima should be used in line with its registered indications and the clinical criteria in the checklists for MAF applications for anti-tumour necrosis factor alpha (anti-TNFα) biologics.

*Published on 1 March 2018*
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 Remsima for rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, chronic plaque psoriasis, 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 Remsima 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
   - 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 A biosimilar is a biological therapeutic product with proven similar physicochemical characteristics, biological activity, safety and efficacy to the reference biological product. The Committee noted that biologics had a high expenditure growth rate of 51% over the last three years and acknowledged that biosimilars would play an important role in improving patient affordability and access to these treatments.

2.2 Remsima is a biosimilar of infliximab (a biological TNF inhibitor) and its reference biologic is Remicade, which was listed on the MAF for all of the indications under evaluation for Remsima at the time of the evaluation.
2.3 In line with local and international clinical guidelines, infliximab is used as a treatment option for patients with moderate to severe rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, plaque psoriasis, ulcerative colitis and Crohn’s disease, who are intolerant of or whose condition has had an inadequate response to conventional disease-modifying anti-rheumatic drugs (DMARDs). The Committee acknowledged expert advice that in local clinical practice, approximately 70% of infliximab use is for ulcerative colitis and Crohn’s disease.

Clinical effectiveness and safety

3.1 The Committee discussed the clinical effectiveness of Remsima and noted that three head-to-head randomised controlled trials (RCT) in patients with rheumatoid arthritis (PLANETRA trial), ankylosing spondylitis (PLANETRAS trial) or Crohn’s disease (NCT02096861) showed comparable efficacy and safety outcomes between Remsima and Remicade up to 54 weeks.

3.2 The Committee also considered results from a phase IV, randomised non-inferiority study (NOR-SWITCH) which included patients, across all licenced therapeutic indications from 40 centres in Norway, and showed that switching from Remicade to Remsima did not worsen the patients’ disease or compromise their safety at 52 weeks.

3.3 The Committee reviewed results from several prospective non-randomised trials which demonstrated comparable efficacy and safety outcomes for Remsima and Remicade in both adults and children who either initiated treatment with Remsima or switched to Remsima once their condition was stable on Remicade. In particular, it noted real-world evidence results from the PROSIT-BIO observational study in which 18% (n=97) of enrolled patients with ulcerative colitis or Crohn’s disease were switched from Remicade to Remsima and had comparable clinical responses to patients who were either treatment naïve to anti-TNFα treatment at enrolment or to patients who had been previously exposed to one or more biologics. Remsima was also shown to have a comparable safety profile to Remicade over the duration of the study.

3.4 On the basis of all available evidence, the Committee concluded that Remsima was clinically comparable to Remicade across all registered indications in patients who initiated treatment with Remsima, or switched from Remicade, once their condition was stable.
Cost effectiveness

4.1 The Committee acknowledged that published economic studies covering 11 European countries reported substantial cost avoidance when new patients were treated with Remsima, or existing patients were switched from Remicade.

4.2 The Committee agreed that a cost-minimisation analysis was appropriate to assess the cost effectiveness of Remsima, in view of its comparable efficacy and safety with Remicade.

4.3 The Committee acknowledged that the price proposed by the manufacturer for Remsima was substantially lower than Remicade’s price, and therefore concluded that it represented a cost-effective treatment option in Singapore.

4.4 In view of the large price differential between Remsima and Remicade, the Committee considered that there was insufficient justification to retain Remicade on the MAF.

Estimated annual technology cost

5.1 The Committee estimated that around 130 people in Singapore across all registered indications would benefit from government assistance for Remsima. No additional annual cost impact to the government was estimated in the first year of listing on the MAF due to potential cost savings from patients initiating treatment with Remsima instead of Remicade, or switching from Remicade to Remsima. The Committee acknowledged that due to improved treatment affordability with Remsima, the number of patients accessing infliximab was likely to increase over time.
Additional considerations

6.1 The Committee noted position statements from international professional bodies on the use of biosimilars for rheumatology and gastrointestinal disorders which recommended that switching to a biosimilar should be on a case-by-case basis and upon clinician’s discussion with the patient. They further considered local expert advice (from gastroenterology, rheumatology and dermatology disciplines) which confirmed that clinicians in Singapore were generally in favour of starting Remsima in new patients who require treatment with infliximab, and would consider actively switching patients whose condition was stable on Remicade if the price difference between the products was significant and treatment affordability was a concern for the patient.

6.2 The Committee agreed that switching between products should be based on clinical judgement, however they advised that clinicians should actively assess each patient’s suitability for switching and provide relevant counsel to patients by taking into consideration the large difference in patient co-payments between Remicade and Remsima.

Recommendation

7.1 On the basis of the evidence available, the Committee recommended infliximab biosimilar (Remsima) 100mg vial for listing on the MAF in line with its registered indications for the treatment of moderately to severely active rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, plaque psoriasis, ulcerative colitis and Crohn’s disease, due to comparable clinical effectiveness and safety with Remicade, and favourable cost-effectiveness.

7.2 The Committee also recommended that infliximab reference biologic (Remicade) should be removed from the MAF for all indications. Clinicians should actively assess each patient’s suitability for switching and provide relevant counsel to patients by taking into consideration the large price difference between Remicade and Remsima. Switching to Remsima or to an alternative subsidised treatment should be done by 31 December 2018, before subsidy for Remicade is completely 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

© Agency for Care Effectiveness, Ministry of Health, Republic of Singapore
All rights reserved. Reproduction of this publication in whole or in part in any material form is prohibited without the prior written permission of the copyright holder. Application to reproduce any part of this publication should be addressed to:

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

In citation, please credit the Ministry of Health when you extract and use the information or data from the publication.