CDEC FINAL RECOMMENDATION

GOLIMUMAB
(Simponi IV — Janssen Inc.)
Indication: Rheumatoid Arthritis

Recommendation:
The Canadian Drug Expert Committee (CDEC) recommends that intravenous (IV) golimumab be listed for use in combination with methotrexate (MTX) for the treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) if the following conditions are met:

Conditions:
- List in a manner similar to subcutaneous (SC) golimumab.
- The overall drug plan cost of treatment with IV golimumab should not exceed the overall drug plan cost of treatment with SC golimumab.

Reasons for the Recommendation:
1. One six-month, double-blind, randomized controlled trial (RCT) (GO-FURTHER; N = 592) demonstrated that IV golimumab (2 mg/kg) in combination with MTX was superior to placebo, as measured by the proportion of patients achieving ACR 20 and ACR 50 responses.

2. At the submitted price ($826.86 per single use 50 mg/4.0 mL vial), IV golimumab is less costly than SC golimumab for patients weighing less than 75 kg; however, the IV formulation is more costly than the SC formulation for patients weighing greater than 75 kg.

Background:
Golimumab is a tumour necrosis factor alpha (TNF-alpha) inhibitor. IV golimumab is indicated for use in combination with MTX, in the treatment of adult patients with moderately to severely active RA. IV golimumab is available as a 50 mg/4.0 mL vial and the recommended dose is 2 mg/kg given as a 30-minute IV infusion at weeks zero and four, and then every eight weeks thereafter.

Summary of CDEC Considerations
CDEC considered the following information prepared by the Common Drug Review (CDR): a systematic review of RCTs of IV golimumab, a critique of the manufacturer's pharmacoeconomic evaluation, and patient group-submitted information about outcomes and issues important to individuals living with RA.

Patient Input Information
The following is a summary of information provided by two patient groups that responded to the CDR call for patient input:

- Having a range of treatment options is important and increases the likelihood that individuals with RA will have access to effective medications with manageable side effects.
- Currently available therapies are limited by adverse effects, high cost, and a substantial process for gaining approval from provincial drug plans for coverage.

Clinical Trials
The CDR systematic review included one multi-centre, randomized, double-blind, placebo-controlled phase 3 trial. The GO-FURTHER study evaluated 592 adult patients (18 years or older) diagnosed with moderately to severely active RA (defined as ≥ 6 tender and ≥ 6 swollen joints) for at least 3 months before screening and at baseline, despite concurrent therapy on a stable MTX dose. Patients were randomized in a 2:1 ratio to receive either 2 mg/kg golimumab or placebo administered by IV, each in combination with a stable MTX dose of between ≥ 15 mg/week and ≤ 25 mg/week. Patients were excluded from the study if they had other inflammatory diseases, or had received prior treatment with another biologic response modifier, systemic immunosuppressives, and disease modifying anti-rheumatic drugs (DMARDs) other than MTX, or parenteral corticosteroids during the four weeks before the first administration of study treatment. Patients in the placebo plus MTX group were eligible to crossover to receive 2 mg/kg golimumab at week 16 if they achieved less than 10% improvement in both tender and swollen joint count.

Outcomes
Outcomes were defined a priori in the CDR systematic review protocol. Of these, CDEC discussed the following:

- ACR 20 response — a composite measure of seven elements comprising swollen joint count (66 joints), tender joint count (68 joints), patient's assessment of pain, patient's global assessment of disease activity, physician's global assessment of disease activity, patient's assessment of physical function as measured by the Health Assessment Questionnaire Disability Index (HAQ-DI), and C-reactive protein (CRP). An ACR 20 responder is a patient who achieved an improvement of 20% or more from baseline in both the swollen joint count and the tender joint count, and a 20% improvement in at least three of the remaining five parameters.
- ACR 50 response — defined as the proportion of patients with improvement of 50% or more from baseline in both the swollen joint count (66 joints) and the tender joint count (68 joints), and a 50% or more improvement in at least three of the remaining five parameters.

- Disease Activity Score in 28 Joints (DAS 28) — an index combining tender joints (28 joints), swollen joints (28 joints), CRP, and global assessment of disease activity.
- HAQ-DI — an index composed of 8 categories: dressing and grooming, arising, eating, walking, hygiene, reach, grip, and activities.
- SF-36 — an instrument comprised of 36 questions evaluating functional health and well-being scores, as well as psychometrically based physical component scores (PCS) and mental component scores (MCS) were used to assess patients' health-related quality of life.
- Total adverse events, serious adverse events, and withdrawals due to adverse events.

The primary efficacy outcome of the GO-FURTHER study was ACR 20 response at week 14.

Efficacy

- Compared with placebo, a statistically significantly greater proportion of patients who received golimumab plus MTX achieved an ACR 20 response at week 14 (58.5% versus 24.9%; $P < 0.001$) and an ACR 50 response at week 24 (34.9% versus 13.2%; $P < 0.001$).
- The proportion of patients who achieved a DAS 28 response of "good" or "moderate" at week 14 was statistically significantly greater with golimumab plus MTX compared with placebo plus MTX (81.3% versus 40.1%; $P < 0.001$). Patients in the golimumab plus MTX treatment group also had greater DAS 28 remission compared with the placebo plus MTX treatment group at week 14 (15.4% versus 4.6%; $P < 0.001$) and at week 24 (17.7% versus 5.1%; $P < 0.001$).
- A greater proportion of patients in the golimumab plus MTX group achieved clinically and statistically significant improvement in HAQ-DI scores at week 14 compared with those in the placebo group. Clinically meaningful improvement in HAQ-DI (≥ 0.25) from baseline was achieved by 68.4% of patients in the golimumab plus MTX group compared with 43.1% in the placebo plus MTX group ($P < 0.001$).
- The median changes from baseline in both SF-36 PCS and MCS scores were statistically significantly greater in the golimumab plus MTX group than in the placebo plus MTX group at weeks 12, 16, and 24 ($P < 0.001$).

Harms (Safety and Tolerability)

- The proportion of patients with at least one adverse event was reported at week 16 (before early escape) and at week 24 (end of the double-blind phase):
  - Week 16: 47.3% with golimumab plus MTX and 43.7% with placebo plus MTX.
  - Week 24: 57.2% with golimumab plus MTX and 49.2% with placebo plus MTX.
- The most commonly reported adverse events were infections and infestations.
- Withdrawals due to adverse events were reported as follows:
  - Week 16: 2.0% with golimumab plus MTX and 1.0% with placebo plus MTX.
  - Week 24: 2.3% with golimumab plus MTX and 1.0% with placebo plus MTX.
- The proportion of patients with at least one serious adverse event was reported as follows:
  - Week 16: 3.8% with golimumab plus MTX and 1.0% with placebo plus MTX.
  - Week 24: 4.8% with golimumab plus MTX and 2.0% with placebo plus MTX.

Cost and Cost-Effectiveness

The manufacturer submitted a cost-minimization analysis, considering only drug costs, of IV golimumab compared with SC golimumab, IV Infliximab, or IV abatacept based on an average patient weight of 75 kg. The manufacturer reported IV golimumab was cost-saving compared

with SC golimumab, IV infliximab, and IV abatacept during the first three years of treatment, representing savings of $4,208 (7.6%), $16,056 (23.9%), and $9,982 (16.3%) respectively, for patients weighing 75 kg.

CDR identified a number of limitations, the most significant of which was assuming an average weight of 75 kg for the analysis rather than using a range of plausible patient weights. CADTH recalculated costs accounting for drug wastage of single use vials, updated drug prices, and a range of patient weights as well as the inclusion of other relevant comparators. Based on the submitted price of IV golimumab, $826.86 per single use 50 mg/4.0 mL vial, at the recommended doses for patients who weigh between 75 kg and 80 kg (2 mg/kg weeks 0 and 4, then every 8 weeks thereafter), IV golimumab costs $23,152 in the first year and $21,498 thereafter. It is more expensive than SC golimumab (50 mg monthly; $18,243 annually), IV abatacept (250 mg at weeks 0, 2, and 4, and every 4 weeks thereafter; $20,177 per patient in year one and $18,736 thereafter), SC adalimumab (40 mg monthly; $19,249 annually), IV etanercept (50 mg weekly; $20,208 annually), and SC certolizumab (400 mg at weeks 0, 2, 4, then 200 mg every 2 weeks; $19,271 in the first year and $17,277 thereafter). IV infliximab (3 mg/kg at weeks 0, 2, 6, and every 8 weeks thereafter) costs $23,701 per patient in year one and $19,257 thereafter; for patients who require the upper range of dosing (10 mg/kg up to every 4 weeks), IV infliximab costs $102,706 per patient per year. CADTH estimated that the price of IV golimumab would need to be reduced by 17.8% to be in line with the least expensive treatments (SC golimumab, SC certolizumab) for patients with average weight < 100 kg, or by 34.5% for patients weighing ≥ 100 kg but < 120 kg to be in line with SC certolizumab.

Other Discussion Points:

CDEC noted the following:

- The placebo phase of the GO-FURTHER trial was limited to 24 weeks in duration.
- The study did not compare against a combination of other DMARDs at optimal doses, which is an alternative to patients not controlled on MTX.

Research Gaps:

- There are no head-to-head trials comparing IV golimumab against other available biologics, including SC golimumab, for the treatment of RA.

CDEC Members:

Dr. Robert Peterson (Chair), Dr. Lindsay Nicolle (Vice-Chair), Dr. Ahmed Bayoumi, Dr. Bruce Carleton, Ms. Cate Dobhran, Mr. Frank Gavin, Dr. John Hawboldt, Dr. Peter Jamieson, Dr. Kerry Mansell, Dr. Irvin Mayers, Dr. Yvonne Shevchuk, Dr. James Silvius, and Dr. Adil Virani.

June 18, 2014 Meeting

Regrets:

None

Conflicts of Interest:

None

About This Document:
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The manufacturer has reviewed this document and has not requested the removal of confidential information in conformity with the *CDR Confidentiality Guidelines*.

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