CEDAC FINAL RECOMMENDATION

GOLIMUMAB
(Simponi – Schering Plough Inc.)
Indication: Psoriatic Arthritis

Recommendation:
The Canadian Expert Drug Advisory Committee (CEDAC) recommends that golimumab be listed in a similar manner to other tumor necrosis factor alpha inhibitors for moderate to severe psoriatic arthritis.

Golimumab dosing should be restricted to a maximum of 50 mg once a month. Response to golimumab should be assessed after 14 to 16 weeks of treatment and therapy be continued only if there is a clinical response.

Reasons for the Recommendation:
1. In the one 24-week, double-blind randomized controlled trial included in the CDR systematic review, golimumab 50 mg was statistically significantly better than placebo with respect to the proportion of patients with moderate to severe psoriatic arthritis achieving an ACR 20, ACR 50 and ACR 70 response as well as other outcomes measuring improvement in psoriatic arthritis symptoms.
2. The annual cost of golimumab is less than the cost of other tumor necrosis factor alpha inhibitors used to treat psoriatic arthritis when it is administered 12 times per year.

Of Note:
The Committee noted that while there are three other tumor necrosis factor (TNF) alpha inhibitors available for the treatment of psoriatic arthritis, there are no head-to-head trials of golimumab compared with these other TNF alpha inhibitors.

Background:
Golimumab is a human monoclonal antibody to TNF alpha with a Health Canada indication for reducing the signs and symptoms in adult patients with moderately to severely active psoriatic arthritis, alone or in combination with methotrexate. It can be used in combination with methotrexate in those who have not responded adequately to methotrexate alone. This indication is the focus of this recommendation. Golimumab also has the following Health Canada indications:

- in combination with methotrexate, for reducing signs and symptoms of adult patients with moderately to severely active rheumatoid arthritis;
- for reducing signs and symptoms of adult patients with active ankylosing spondylitis who have had an inadequate response to conventional therapies.

The Health Canada recommended dose of golimumab for psoriatic arthritis is 50 mg given as a subcutaneous injection once a month on the same date each month. It is available as an autoinjector and as a prefilled syringe containing golimumab 50 mg in 0.5 mL of solution.

Summary of CEDAC Considerations:
The Committee considered the following information prepared by the Common Drug Review (CDR): a systematic review of double-blind randomized controlled trials (RCTs) of golimumab and a critique of the manufacturer's pharmacoeconomic evaluation.

Clinical Trials
The CDR systematic review included one manufacturer-sponsored, double-blind, 24-week randomized placebo-controlled trial, GO-REVEAL (N = 405), evaluating the efficacy of golimumab 50 mg and golimumab 100 mg. Golimumab was administered every four weeks. The patients who were enrolled had at least three tender and three swollen joints, and had active disease despite therapy with disease-modifying anti-rheumatic drugs (DMARDs) and/or non-steroidal anti-inflammatory drugs (NSAIDs). All patients were TNF alpha inhibitor naive. Approximately 47% to 49% of patients received concomitant methotrexate during the trial and 75% to 78% received NSAIDs.

At 16 weeks, patients with less than 10% improvement from baseline in both swollen and tender joint counts met the early escape criteria (45%, 19%, and 17% of placebo, golimumab 50 mg, and golimumab 100 mg patients, respectively). Patients meeting the early escape criteria in the placebo group began receiving golimumab 50 mg, those in the 50 mg group had their dose escalated to golimumab 100 mg and those in the 100 mg group continued receiving 100 mg golimumab. Entry into early escape was double-blinded. There were an additional 2.7% to 10.6% of patients across treatment groups who discontinued treatment by week 24. Patients who met the early escape criteria at week 16 had their week 14 values carried forward for the week 24 analyses.

Outcomes
The co-primary outcomes of the trial were the proportion of patients with at least 20% improvement in the American College of Rheumatology (ACR 20) criteria at week 14 and the change from baseline in van der Heijde modified Sharp score (vdH-S) at week 24.

The ACR criteria include the following components: swollen joint counts; tender joint counts; patient global assessment of disease activity; physician assessment of disease activity; patient assessment of pain; physical function as assessed by the Health Assessment Questionnaire (HAQ); and either C-reactive protein levels or erythrocyte sedimentation rates. Patients are considered ACR 20 responders if they have a 20% improvement from baseline in swollen and tender joint counts plus a 20% improvement in three of the five other components.

The vdH-S scale, also known as the modified Sharp scale, measures radiographic progression and has scores ranging from zero to 440, with higher scores indicating greater disease severity. A clinically relevant difference in the vdH-S scale has not been established for patients with psoriatic arthritis.

Other outcomes were defined a priori in the CDR systematic review protocol. Of these outcomes, the Committee discussed the following: ACR 50, ACR 70, enthesitis and dactylitis assessments, Psoriatic Arthritis Response Criteria (PsARC), Disease Activity Score for 28 joints (DAS28), the HAQ, morning stiffness, Psoriasis Area and Severity Index (PASI) response, Nail Psoriasis Severity Index (NAPSI) response, work productivity and quality of life as measured using the SF-36.

Results

Efficacy or Effectiveness

- The co-primary endpoints of GO-REVEAL were both achieved. There was a statistically significantly greater proportion of ACR 20 responders in the golimumab 50 mg group compared with placebo at week 14 (51% versus 9%, $P < 0.001$). Golimumab 50 mg significantly inhibited radiographic progression compared with placebo at week 24 (-0.16 versus 0.27, respectively, $P < 0.01$).
- Statistically significant improvements favouring golimumab 50 mg over placebo were observed at weeks 14 and 24 for additional outcomes measuring the signs and symptoms of psoriatic arthritis including ACR 50, ACR 70, PASI 75, PsARC, DAS28-CRP responders, HAQ, SF-36, NAPSI and enthesitis scores measured by the modified Maastricht Ankylosing Spondylitis Enthesitis Score (mMASES).
- The change from baseline in dactylitis scores and time lost from work were similar between the golimumab 50 mg and placebo groups.
- Efficacy appeared similar between 50 mg and 100 mg golimumab doses for most outcomes and similar proportions of patients in the 50 mg and 100 mg groups met the early escape criteria at week 16 (19% and 17% respectively). Among the patients who met the early escape criteria and had their golimumab dose escalated from 50 mg to 100 mg, only 14% achieved ACR 20 at week 24, while 16% of patients who met the early escape criteria and remained on golimumab 100 mg achieved ACR 20 at week 24.

Harms (Safety and Tolerability)

- The proportion of patients with serious adverse events (2.1% versus 6.2% respectively), adverse events (67.8% versus 59.3% respectively) and withdrawals due to adverse events (4.4% versus 1.4% respectively) was similar between the golimumab 50 mg and placebo groups at week 24. Very few adverse events occurred between week 14 and week 24 for patients meeting early escape criteria. Twenty-four weeks was considered a short duration for controlled assessment of harms given that psoriatic arthritis is a chronic disease.
- Infections and malignancies appeared similar between golimumab 50 mg and placebo. More patients in the placebo group had a serious infection than patients in the golimumab 50 mg group (3.5% versus 0.7% respectively). There were no cases of active tuberculosis observed in the study. Three malignancies were reported (2.0%), and all of them were in the golimumab 100 mg group.

Cost and Cost-Effectiveness
The manufacturer submitted a cost-utility analysis looking at TNF alpha inhibitors (golimumab, etanercept, adalimumab and infliximab) compared with supportive care (i.e., DMARDs) in patients with psoriatic arthritis who are refractory to DMARDs. The economic evaluation was based on a published model. Estimates of clinical effectiveness were based on an indirect comparison conducted by the manufacturer, which considered three outcome measures obtained from placebo-controlled trials evaluating TNF alpha inhibitors (PsARC response, change in HAQ score, and change in PASI score). The Committee placed more emphasis on the costs of golimumab and comparators. The annual cost of treatment with golimumab ($17,364; 50 mg monthly) is less than etanercept ($18,995; 50 mg weekly or $20,542; 25 mg twice weekly), adalimumab ($18,438; 40 mg every other week), and infliximab ($20,538; 5 mg/kg every eight weeks based on a 70 kg patient).

Other Discussion Points:
- The Health Canada recommended dosing regimen is golimumab 50 mg once a month (12 doses per year) but the regimen evaluated in clinical trials is golimumab 50 mg every four weeks (13 doses per year). If golimumab was administered 13 times per year, its cost would be more similar to other TNF alpha inhibitors.
- The maximum duration of therapy of golimumab is unknown.
- There is insufficient evidence to assess the long-term harms associated with golimumab.
- There are currently no RCTs evaluating the effectiveness of golimumab in patients with psoriatic arthritis who have failed other TNF alpha inhibitors.

CEDAC Members Participating:
Dr. Robert Peterson (Chair), Dr. Michael Allan, Dr. Ken Bassett, Dr. Bruce Carleton, Dr. Doug Coyle, Mr. John Deven, Dr. Alan Forster, Dr. Laurie Mallery, Mr. Brad Neubauer, Dr. Lindsay Nicolle, and Dr. Kelly Zarnke.

Regrets:
Dr. Anne Holbrook (Vice-Chair) and Dr. Yvonne Shevchuk.

Conflicts of Interest:
One CEDAC member reported a conflict of interest and did not participate in the vote.

About this Document:
CEDAC provides formulary listing recommendations to publicly funded drug plans. Both a technical recommendation and plain language version of the recommendation are posted on the CADTH website when available.

CDR clinical and pharmacoeconomic reviews are based on published and unpublished information available up to the time that CEDAC made its recommendation.

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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