CEDAC FINAL RECOMMENDATION on RECONSIDERATION and REASONS for RECOMMENDATION

ABATACEPT
(Orencia™ – Bristol-Myers Squibb Canada)

Description:
Abatacept is a soluble fusion protein that selectively modulates a key co-stimulatory pathway required for full activation of T lymphocytes expressing CD28. Abatacept is approved for use in reducing signs and symptoms, inducing clinical responses, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more disease modifying anti-rheumatic drugs (DMARDs) and/or to anti-tumour necrosis factor (anti-TNF) therapies.

Dosage Forms:
250 mg vial for intravenous injection. Abatacept is administered as a 30 minute intravenous infusion at the doses of 500mg for patients weighing <60kg, 750mg for patients weighing 60 to 100kg, and 1g for those weighing >100kg. Abatacept should be given at 2 and 4 weeks after the first infusion and then every 4 weeks thereafter.

Recommendation:
The Canadian Expert Drug Advisory Committee (CEDAC) recommends that abatacept, used in combination with DMARDs (when these agents are not contraindicated), be listed for the treatment of patients with severely active rheumatoid arthritis who have failed to respond to an adequate trial of an anti-TNF agent. Abatacept should not be used in combination with anti-TNF agents.

Reasons for the Recommendation:
1. When added to methotrexate, abatacept has been shown to be more effective than placebo in patients with rheumatoid arthritis who have failed DMARDs and in patients who have failed anti-TNF therapy.

2. There is insufficient evidence that abatacept is superior to other biologic therapies (eg. anti-TNF therapies, rituximab) in rheumatoid arthritis and there is more clinical experience with the use of anti-TNF therapies.

Summary of Committee Considerations:

The Committee considered a systematic review of randomized controlled trials (RCTs) of abatacept in adults with rheumatoid arthritis who had an inadequate response to one or more DMARDs or anti-TNF therapies. Five double blind, placebo controlled RCTs, lasting from six months to one year in duration, met the inclusion criteria for the systematic review – three of these were in patients who had failed DMARDs (one of these also included a treatment arm with infliximab), one was in patients who had failed prior anti-TNF therapy and one was in patients who had failed prior DMARDs and/or biologic therapies. The primary outcome of the latter RCT was to assess the safety of abatacept and efficacy outcomes were not reported. Patients in all trials were maintained on background DMARD therapy.

In the RCTs in patients who had failed prior DMARD therapy, the addition of abatacept to methotrexate resulted in significantly more patients achieving 20%, 50% and 70% improvements in the American College of Rheumatology response criteria (ACR 20, ACR 50 and ACR 70) compared to the addition of placebo to methotrexate therapy. The numbers needed to treat (NNT) to achieve ACR 70 response at one year ranged from 5 to 8. Statistically significant changes of similar magnitude, in comparison to placebo, were also reported in the Disease Activity Score on 28 joints (DAS28) and the Health Assessment Questionnaire (HAQ) scores. Quality of life was also significantly improved with abatacept. In the one RCT that compared abatacept to infliximab, similar results were reported with these treatments.

In the RCT in patients who had failed anti-TNF therapy, abatacept resulted in significantly more patients achieving ACR 20 (NNT=4), ACR 50 (NNT=6) and ACR 70 (NNT=12) at one year compared to placebo. Abatacept also resulted in statistically significant improvements in DAS28, HAQ scores and quality of life.

Serious infections can occur during therapy with abatacept. The combination of abatacept with other biologic agents in rheumatoid arthritis is not recommended due to the increased risk of serious infection. The most common adverse events reported in patients receiving abatacept were headache, nasopharyngitis and nausea.

Abatacept costs approximately $17,000 to $23,000 per year, which is similar to anti-TNF therapies.

Of Note:

1. Both published and unpublished data were reviewed and taken into consideration in making this recommendation.

2. The Committee recommends that drugs plans consider a drug class review of biologic therapies in rheumatoid arthritis.

Background:

CEDAC provides formulary listing recommendations to publicly funded drug plans. Recommendations are based on an evidence-based review of the medication's effectiveness and safety and an assessment of its cost-effectiveness in comparison to other available treatment options. For example, if a new medication is more expensive than other treatments, the Committee considers whether any advantages of the new medication justify the higher price. If the recommendation is not to list a drug, the Committee has concerns regarding the balance between benefit and harm for the medication, and/or concerns about whether the medication provides good value for public drug plans.