Canadian Agency for Drugs and Technologies in Health | Agence canadienne des médicaments et des technologies de la santé

CEDAC FINAL RECOMMENDATION on RECONSIDERATION and REASONS for RECOMMENDATION

EFALIZUMAB
(Raptiva® – Serono Canada Inc.)

This product has been withdrawn from the Canadian market.
Date of notification was June 8, 2009.

Description:
Efalizumab is a recombinant humanized monoclonal antibody that binds specifically to the CD11a subunit of LFA-1 (lymphocyte function-associated antigen-1) and interferes with T-lymphocyte adhesion to other cell types. It is approved for use in the treatment of moderate to severe chronic plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy. Efalizumab is administered by subcutaneous injection at a dose of 1 mg/kg weekly.

Dosage Forms:
150 mg vial for subcutaneous injection

Recommendation:
The Canadian Expert Drug Advisory Committee (CEDAC) recommends that efalizumab be listed for patients with severe, debilitating psoriasis who meet all of the following criteria.

1. Body surface area (BSA) involvement of >10% and/or significant involvement of the face, hands, feet or genital region;
2. Failure to respond to, contraindications to, or intolerant of methotrexate and cyclosporine;
3. Failure to respond to, intolerant to or unable to access phototherapy;
4. Entry into a registry, the principles of which are described below.

Response to efalizumab must be assessed after 12 weeks, and therapy continued only in patients who have responded to therapy. Potential criteria for defining response are patients who have achieved a ≥75% reduction in Psoriasis Area Severity Index (PASI) score, or a ≥50% reduction in PASI with a ≥5 point improvement in the Dermatology Life Quality Index (DLQI) or a quantitative reduction in BSA affected with qualitative consideration of specific regions such as face, hands, feet or genital region.

The Committee recommends that all patients who meet the first three criteria above be entered into a registry to collect effectiveness and harm outcome information on patients that are responders, partial responders and non-responders to efalizumab therapy. Patient follow-up must continue for a minimum of 12 weeks after efalizumab is discontinued and an annual summary of patient outcomes must be made available to drug plans (and preferably disclosed publicly). In all aspects of the registry, patient confidentiality must be maintained. The oversight for such a registry must have sufficient independence to ensure impartiality.

Reasons for the Recommendation:

1. The Committee considered the results of three, 12 week double-blind randomized controlled trials (RCTs) comparing efalizumab to placebo in adult patients with moderate to severe plaque psoriasis. Efalizumab treatment was associated with statistically significant and clinically important improvements in PASI score, Physician Global Assessment of response, Patient Global Psoriasis Assessment and DLQI scores. In one RCT that enrolled a subgroup of patients who had failed or had contraindications to two or more systemic therapies, the efficacy of efalizumab was maintained in this group of patients. No RCT compared efalizumab to other systemic drug treatments.

2. In one RCT which followed patients after discontinuation of efalizumab treatment, rebound (as defined by a 25% deterioration in PASI score compared with baseline) was seen in 9.1, 14.4% and 29.8% of responders, partial responders and non-responders, respectively. Patient follow-up from the other two RCTs was inadequate to permit an assessment of the rate of rebound and the Committee was concerned about the potential for significant worsening of psoriasis after discontinuation of efalizumab, especially in patients who are partial or non-responders.

3. The most serious adverse effects observed during treatment with efalizumab therapy were serious infections, malignancies, thrombocytopenia and haemolytic anemia. Data from the RCTs reported significantly higher rates of total adverse events, withdrawals due to adverse events and infection-related adverse events in efalizumab treated patients.

4. The RCTs of efalizumab have been of relatively short duration, therefore its long-term effectiveness and safety is unclear. A registry will provide useful information on the nature and incidence of serious adverse events and on the effectiveness of efalizumab beyond 12 weeks of therapy.

5. One year of treatment with efalizumab costs approximately $21,000. An economic analysis submitted by the manufacturer compared efalizumab to standard care but the Committee felt that this analysis overestimated the efficacy and underestimated the costs of efalizumab relative to standard care. The manufacturer has requested that the cost per quality-adjusted life year from this analysis remain confidential pursuant to the Confidentiality Guidelines of the Procedure for the Common Drug Review.

Of Note:

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

2. Based on data from the registry, drug plans will seek further advice from the Committee on the role of efalizumab.

3. A number of biologic agents are now approved for use in severe psoriasis. Drug plans should consider a drug class review of these agents to assess their relative effectiveness, harms, cost and place in therapy and, the role of registries for these drugs.