

Committee to Evaluate Drugs (CED)

Recommendations and Reasons

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Tocilizumab for juvenile arthritis

Product: tocilizumab (Actemra®)

Class of Drugs: interleukin-6 (IL-6) receptor inhibitor

Reason for Use: polyarticular juvenile idiopathic arthritis (pJIA)

Manufacturer: Hoffmann-La Roche Limited

Date of Review: April 9, 2014

CED Recommendation

The CED recommended tocilizumab (Actemra®) be funded for the treatment of polyarticular juvenile idiopathic arthritis (pJIA) according to specific criteria. The evidence shows tocilizumab is superior to placebo for reducing disease flare in children with pJIA and the cost compares reasonably to alternative agents.

Executive Officer Decision*

Based on the CED's recommendation and an agreement with the manufacturer, the Executive Officer decided to fund tocilizumab (Actemra®) for pJIA according to specific criteria.

Funding Status*

Funded through the Ontario Drug Benefit's Exceptional Access Program according to specific criteria.

(EAP criteria can be found at: http://www.health.gov.on.ca/en/pro/programs/drugs/eap_criteria.aspx)

** This information is current as of the posting date of the document. For the most up-to-date information on Executive Officer decision and funding status, see: www.health.gov.on.ca/en/pro/programs/drugs/status_single_source_subm.aspx.*

Highlights of Recommendation:

- Tocilizumab was shown in a clinical study to be superior to placebo for reducing the occurrence of disease flare in children with polyarticular juvenile idiopathic arthritis (pJIA).
- Indirect evidence suggests that tocilizumab is similar in efficacy as comparator biologic treatments for pJIA.
- There is a lack of long-term data on the effectiveness and safety of tocilizumab.
- Tocilizumab costs approximately \$7,000 to \$13,000 per year, depending on the patient's body weight. It is less expensive than alternative biologic agents for patients who weigh between 34-75 kg.

Background:

Juvenile idiopathic arthritis (JIA) is a type of arthritis of unknown cause that begins before the age of 16. Symptoms of JIA include joint swelling, pain, stiffness, and loss of motion. JIA can affect any joint, and in some cases it can affect internal organs as well. There are three major categories of JIA: polyarticular JIA (pJIA), systemic JIA (sJIA) and enthesitis-related arthritis (ERA).

Commonly used therapies for JIA include nonsteroidal anti-inflammatory drugs (NSAIDs), disease-modifying antirheumatic drugs (DMARDs), and biologic agents.

Tocilizumab is a biologic agent belonging to a class of drugs called interleukin-6 (IL-6) receptor inhibitor.

Detailed Discussions:

- For this evaluation, the CED considered:
 - Findings from the Common Drug Review (CDR) and the recommendation of the Canadian Drug Expert Committee (CDEC);
 - Information in the manufacturer's submission;
 - Three patient group submissions.
- One randomized, double-blind, placebo-controlled trial, the CHERISH study, evaluated the efficacy and safety of tocilizumab, as monotherapy or in combination with methotrexate (MTX), in patients with active pJIA who had previously experienced an inadequate response or intolerance to MTX. After an initial 16-week lead-in phase where all patients received tocilizumab, patients that responded to the treatment then entered the double-blind phase where they received either tocilizumab or placebo.
- The primary efficacy outcome was the proportion of patients whose disease worsened relative to week 16 (i.e., JIA ACR30 flare). The study also measured the proportion of patients who experienced measurable improvements (i.e., JIA ACR30/50/70/90 responses).
- The proportion of patients who worsened (i.e., experienced an ACR30 flare) was statistically significantly less in the tocilizumab group compared with the placebo group (25.6% versus 48.1%; 95% CI, -0.35 to -0.08).

- The proportion of patients who improved (i.e., demonstrated ACR 30 response) was statistically significantly greater in the tocilizumab group compared with the placebo group (74.4% versus 54.3%; 95% CI, 0.05 to 0.33).
- The proportion of patients that reported at least one adverse event was 74.1% in the placebo group and 70.7% in the tocilizumab group. The most frequently reported adverse events in tocilizumab-treated patients were inflammation of the throat and nasal passages, headache, and upper respiratory tract infection. A higher proportion of patients reported an infection with tocilizumab than with placebo (43.9% versus 38.3% respectively).
- The CED noted that one of the limitations of the CHERISH study is that it included only patients who achieved an ACR30 response during the 16-week lead-in period. This may have biased the results in favour of tocilizumab.
- Patients in the study received five months of treatment. The CED noted that long-term data on efficacy, patients' quality of life, and safety are lacking.
- There are no direct comparison studies between tocilizumab and other biologic agents used to treat pJIA. Indirect comparisons appear to suggest that there are no significant differences in efficacy among the various biologic treatments for this condition.
- Tocilizumab costs approximately \$7,000 to \$13,000 per year, depending on the patient's body weight. Tocilizumab is less expensive than other biologic agents for patients who weigh between 34-75 kg. Because tocilizumab is administered by intravenous infusion, the Committee noted that there will likely be extra administrative costs associated with treatment (e.g., infusion clinics, nursing time).
- The CED considered three patient group submissions and noted tocilizumab requires less frequent administration compared with other biologic treatments and may provide added patient convenience.
- Overall, tocilizumab has been shown to be superior to placebo for reducing the occurrence of disease flare in children with pJIA. Tocilizumab appears to be similar in efficacy as other biologic treatments for pJIA and it is less costly for patients weighing 34-75kg.

Committee to Evaluate Drugs (CED)

The Committee to Evaluate Drugs (CED) is comprised of practicing physicians, pharmacists, health economists, and patient representatives. In conducting its review, the CED considers data contained in the drug manufacturer's submission, input provided by patient groups, findings from the national Common Drug Review and the pan-Canadian Oncology Drug Review, and other scientific information as necessary.

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