CEDAC FINAL RECOMMENDATION on RECONSIDERATION and REASONS for RECOMMENDATION

LUMIRACOXIB
(Prexige™ – Novartis Pharmaceuticals Canada Inc.)

This product has been withdrawn from the Canadian market.
Date of notification was October 3, 2007.

Description:
Lumiracoxib is a nonsteroidal anti-inflammatory drug (NSAID) with selective activity against cyclooxygenase-2 (COX-2). It is approved for the acute and chronic treatment of the signs and symptoms of osteoarthritis of the knee in adults.

Dosage Forms:
100 mg tablets. The recommended dose is 100 mg once daily.

Recommendation:
The Canadian Expert Drug Advisory Committee (CEDAC) recommends that lumiracoxib not be listed.

Reasons for the Recommendation:
1. Lumiracoxib costs $1.17 per day which is more than generic forms of NSAIDs such as naproxen ($0.21 – 0.42 per day) and ibuprofen ($0.05 – 0.19 per day) but less than celecoxib ($1.30 per day). While there is evidence that lumiracoxib is associated with fewer gastrointestinal (GI) complications than other NSAIDs, there is the potential for increased cardiovascular risk compared to naproxen. Since death and hospitalization from cardiovascular disease are more common than from GI complications, the Committee was concerned that the use of lumiracoxib could lead to more harm than benefit.
2. The economic evaluation submitted by the manufacturer reported that lumiracoxib was most cost-effective in patients at high risk of GI complications and low risk of cardiovascular complications who are not taking acetylsalicylic acid (ASA). However, no clinical trials on the relative safety of lumiracoxib versus other NSAIDs in this target population were provided. Many patients at high risk of GI complications are also elderly and have cardiovascular disease, a group for which other analgesics would be recommended.

Summary of Committee Considerations:

The Committee considered a systematic review of randomized controlled trials (RCTs) in adult patients with osteoarthritis of the knee. Two trials comparing lumiracoxib with celecoxib and placebo, each of 13 weeks duration in a total of 3,235 patients, met the inclusion criteria for the systematic review. Compared with placebo, lumiracoxib resulted in statistically significant improvements in pain intensity, the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and patient global assessment, although the pooled mean differences for each of these on a 100 mm visual analogue scale were modest (6.11, 5.62 and 7.77, respectively). There were no statistically significant differences between lumiracoxib and celecoxib for any outcomes in the RCTs.

The Committee also considered the results of a one year RCT in 18,244 patients, who were not at high risk for cardiovascular disease, that was designed to assess the GI safety of lumiracoxib 400 mg daily compared to naproxen 500 mg twice daily and ibuprofen 800 mg three times daily. The one year incidence of ulcer complications (defined as clinically significant bleeding, perforation or obstruction from an erosive or ulcer disease) was slightly lower in patients taking lumiracoxib (0.32%) compared to those in the combined naproxen and ibuprofen groups (0.91%) (number needed to treat [NNT] of 170. Although not statistically significant, lumiracoxib produced a 48% increase in a composite endpoint of cardiovascular events (confirmed or probable clinical myocardial infarction, silent myocardial infarction, stroke or cardiovascular death) compared to naproxen (0.84% vs 0.57%).

The manufacturer submitted an economic evaluation of lumiracoxib compared to celecoxib and conventional NSAIDs (naproxen, ibuprofen, diclofenac). While lumiracoxib was less expensive and similar in effectiveness to celecoxib, the incremental cost per quality adjusted life year (QALY) gained compared to naproxen ranged from $18,311 in patients not taking ASA who were at high risk of gastrointestinal (GI) complications to $363,516 in patients taking ASA who were at low risk of GI complications. However, limitations were identified with the economic analysis – limited information was available on the comparative safety of lumiracoxib and conventional NSAIDs taken with proton pump inhibitors and the magnitude of clinical benefit with lumiracoxib compared to conventional NSAIDs was small (maximum of 0.04 QALYs over a 5 year time horizon).

Of Note:

1. Both published and unpublished data were reviewed and taken into consideration in making this recommendation.
2. Drug plans should consider a review of COX-2 selective NSAIDs in comparison to less selective NSAIDs in light of recent information on potential differences in the effectiveness, safety and cost-effectiveness of these agents.
3. Although lumiracoxib is less expensive than celecoxib, the Committee was not convinced that listing lumiracoxib would result in savings to overall expenditures on NSAIDs.

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.