CEDAC FINAL RECOMMENDATION on RECONSIDERATION and REASONS for RECOMMENDATION

TRAMADOL HYDROCHLORIDE
(Zytram XL® - Purdue Pharma)

Description:
Zytram XL® is an extended release formulation of tramadol hydrochloride, a synthetic opioid analgesic. It is approved for the management of pain of moderate severity in adults who require treatment for several days or more.

Dosage Forms:
150, 200, 300 and 400 mg tablets. The usual initial dose is 150 mg daily. If adequate pain relief is not achieved, the dosage should be gradually titrated upwards. The maximum recommended daily dose is 400 mg.

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

Reasons for the Recommendation:
1. There is insufficient evidence that Zytram XL® provides a therapeutic advantage over less expensive analgesics.

Summary of Committee Considerations:
The Committee considered a systematic review of double blind, randomized controlled trials (RCTs) of tramadol hydrochloride extended release tablets with other oral opiates available in Canada in the treatment of pain of at least several days duration in adults. One unpublished trial met the inclusion criteria for the systematic review. The manufacturer has requested that information from this trial remain confidential, pursuant to the Confidentiality Guidelines of the Common Drug Review.

Zytram XL® costs $1.60 to $4.00 for doses ranging from 150 mg to 400 mg daily. Given the lack of comparative trials, it is difficult to establish the dose equivalency for Zytram XL relative to other analgesics. The Committee noted that there are short-acting analgesic combination products (e.g. codeine 30 mg/acetaminophen 300 mg, oxycodone 5 mg/acetaminophen 325 mg) and long acting formulations of morphine and non-steroidal anti-inflammatory drugs (NSAIDs) that are less costly than Zytram XL.

Of Note:

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 Both published and unpublished data were reviewed and taken into consideration in making this recommendation.

2. There is no evidence that extended release formulations of tramadol hydrochloride offer a therapeutic advantage over nonsteroidal anti-inflammatory drugs (NSAIDs).

3. While the scheduling of tramadol hydrochloride in Canada has not yet been completed, it is proposed to be scheduled in a similar manner to other opioid analgesics (eg. morphine, codeine, oxycodone), given its potential for abuse and dependence (Canada Gazette Vol. 141, No. 27, July 7, 2007).

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.