CEDAC FINAL RECOMMENDATION on RECONSIDERATION and REASONS for RECOMMENDATION

TRAMADOL HYDROCHLORIDE
(Ralivia™ – Biovail Pharmaceuticals Canada)

Description:
Ralivia™ 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 continuous treatment for several days or more.

Dosage Forms:
100, 200 and 300 mg tablets. The recommended initial dose is 100 mg daily and the maximum recommended daily dose is 300 mg.

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

Reasons for the Recommendation:
1. There is insufficient evidence that Ralivia provides a therapeutic advantage over acetaminophen, codeine, acetaminophen plus codeine or non-steroidal anti-inflammatory drugs (NSAIDs).

2. The cost of Ralivia is significantly higher than acetaminophen, codeine, acetaminophen plus codeine or non-steroidal anti-inflammatory drugs (NSAIDs).

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 for the treatment of pain of at least several days duration in adults. No trials met the inclusion criteria for the systematic review.

The Committee also reviewed the results of published systematic reviews of tramadol in chronic pain conditions which have reported that tramadol is more effective than placebo. These systematic reviews did not assess extended release formulations of tramadol separately.

The Committee considered a 12 week, double blind RCT of Ralivia (100 mg, 200 mg or 300 mg daily), celecoxib (200 mg daily) and placebo in patients with osteoarthritis. Celecoxib was superior to placebo at

12 weeks on all three primary outcomes: Western Ontario and McMaster Universities (WOMAC) pain scores, WOMAC physical function and patient's global assessment of disease activity. Only the 300 mg dose of Ralivia differed from placebo and on only one of the three outcome measures, the patient's global assessment of disease activity. Quality of life scores (SF-36, physical component scale) were statistically significantly higher for celecoxib than Ralivia 300mg (the Ralivia dose with the best outcome). A higher proportion of patients withdrew due to adverse events from Ralivia (all doses combined) than celecoxib.

At the price submitted to the Common Drug Review by the manufacturer, Ralivia is less expensive than some long-acting opioid formulations, such as other tramadol products, oxycodone, and fentanyl, but more costly than other analgesics, such as codeine/acetaminophen, oxycodone/acetaminophen (e.g. codeine 30 mg/acetaminophen 300 mg costs $0.05 per tablet, oxycodone 5 mg/acetaminophen 325 mg costs $0.13 per tablet), long acting formulations of morphine and NSAIDs. The manufacturer has requested that the price of Ralivia submitted to the Common Drug Review 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.

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.