



COMMON DRUG REVIEW

CEDAC FINAL RECOMMENDATION

HYDROMORPHONE HYDROCHLORIDE

(Jurnista – Janssen-Ortho Inc.)

Indication: Chronic Pain

Recommendation:

The Canadian Expert Drug Advisory Committee (CEDAC) recommends that hydromorphone hydrochloride (Jurnista) not be listed at the submitted price.

Reason for the Recommendation:

There is insufficient evidence that Jurnista offers a therapeutic advantage compared with other less costly sustained-acting opioid formulations.

Of Note:

1. Based on a review of the clinical evidence, the Committee felt that a reduced price could improve the cost-effectiveness of Jurnista and, thereby, the likelihood of a recommendation to “list” or “list with criteria.”
2. The Committee considered that there was insufficient evidence regarding less diversion with Jurnista compared with other opioids.
3. The Committee noted the lack of evidence supporting the effect of Jurnista on clinically meaningful outcomes such as quality of life and functional outcomes in patients with chronic pain. The need for a drug class review of sustained-acting opioid formulations in this therapeutic area was noted.

Background:

Jurnista has a Health Canada indication for the management of moderate to severe chronic pain in adults who require around-the-clock opioid analgesia. It is a prolonged-release formulation of a semi-synthetic opioid analgesic.

The Health Canada-recommended initial dose of Jurnista, in patients who are opioid naive or receiving low intermittent doses of weak opioid analgesics, is 4 mg to a maximum of 8 mg every 24 hours. The dose may be titrated upwards or downwards, if required, in increments of either

Common Drug Review

4 mg or 8 mg, depending on response and supplementary analgesic requirements. Tablet strengths of 16 mg and higher are only for opioid-tolerant patients requiring hydromorphone equivalent dosages of 16 mg or higher per day.

Jurnista is available as 4 mg, 8 mg, 16 mg, and 32 mg prolonged-release tablets. A 64 mg tablet has also been approved by Health Canada but is not currently marketed in Canada. Jurnista uses an oral osmotic pump to provide osmotic controlled-release drug delivery.

Summary of CEDAC Considerations:

The Committee considered the following information prepared by the Common Drug Review (CDR): a systematic review of double-blind (DB) randomized controlled trials (RCTs) of Jurnista and a critique of the manufacturer's pharmacoeconomic evaluation.

Clinical Trials

The CDR systematic review of Jurnista included one DB RCT, Study DO-119 (N = 169). It was an unpublished, manufacturer-sponsored, multicentre trial of adult patients with chronic pain. The study had a two-week, open-label, run-in phase during which patients were titrated and stabilized on hydromorphone immediate release. The 113 patients who achieved a stable hydromorphone dose between 20 mg and 60 mg daily and had three or fewer doses of rescue medication per day for two consecutive days were then randomized to continue at the same full dose of hydromorphone using Jurnista (n = 34), receive half their dose of hydromorphone using Jurnista (n = 40), or to continue on the same dose of hydromorphone immediate release (n = 39) for seven days.

Patients who were eligible for the study required strong oral or transdermal opioid analgesics or were suitable for advancement of therapy to step three on the World Health Organization analgesic ladder. The types of pain that patients reported at study enrolment included musculoskeletal (57%), neuropathic (35%), sympathetic (5%), and cancer-related pain (2%). Seven of the 113 patients discontinued the study.

Outcomes

The primary outcome of Study DO-119 was the change in the total daily dose of breakthrough pain medication use, as measured by the total daily dose and the number of daily doses.

Other outcomes were defined a priori in the CDR systematic review protocol. Of these, the Committee discussed the following: reduction in pain and adverse events.

Quality of life, treatment compliance, and functional outcomes were not measured and the study was not designed to measure diversion potential.

Results

Efficacy or Effectiveness

- Breakthrough medication use increased in all three treatment groups, but there were no statistically significant differences between groups. Approximately 61% of patients in the full-dose Jurnista and hydromorphone immediate-release groups and 82% of patients in the

Common Drug Review

half-dose Journista group required increased doses of rescue medication by the end of seven days of treatment compared with baseline.

- There were no statistically significant differences between the three treatment groups for any other efficacy outcomes, including those measuring a reduction in pain.

Harms (Safety and Tolerability)

- Adverse events were similar in the Journista and hydromorphone immediate-release groups. The proportion of patients who withdrew due to an adverse event was 6% in the full-dose Journista group compared with none in the half-dose Journista group and the hydromorphone immediate-release group.
- There was one case of drug abuse reported as a serious adverse event in the 14-day, open-label, run-in phase in the hydromorphone immediate-release group and no cases reported during the seven-day blinded treatment phase.

Cost and Cost-Effectiveness

The manufacturer submitted a cost comparison for Journista based on the assumption of similar efficacy and harms compared with other sustained-acting opioid formulations. No RCTs were cited by the manufacturer or identified in the CDR systematic review to support this assumption.

Journista costs more than hydromorphone hydrochloride (Hydromorph Contin) and all other sustained-acting opioid formulations except oxycodone (Oxycontin). For doses ranging from 4 mg to 32 mg once daily, Journista costs \$0.97 to \$7.76. For doses of Hydromorph Contin ranging from 6 mg to 36 mg (3 mg twice daily to 18 mg twice daily), the daily cost is \$1.26 to \$4.78.

Other Discussion Points:

- It was noted that Journista has not been compared with other sustained-acting opioid formulations in DB RCTs.
- The Committee discussed that Journista is the only sustained-acting hydromorphone formulation that is indicated for use once daily. Once daily oral formulations of opioids are available, but the other sustained-acting formulation of hydromorphone (Hydromorph Contin) is indicated for use every 12 hours. There is no evidence demonstrating improved compliance or quality of life with once daily dosing compared with twice daily dosing of sustained-acting opioid formulations.
- The Committee noted that the patent for OxyContin is scheduled to expire in November 2012.

CEDAC Members Participating:

Dr. Robert Peterson (Chair), Dr. Anne Holbrook (Vice-Chair), Dr. Michael Allan, Dr. Ken Bassett, Dr. Bruce Carleton, Mr. John Deven, Dr. Alan Forster, Dr. Laurie Mallery, Mr. Brad Neubauer, Dr. Lindsay Nicolle, Dr. Yvonne Shevchuk, and Dr. Kelly Zarnke.

Regrets:

Dr. Doug Coyle.

Common Drug Review

Common Drug Review

Conflicts of Interest:

CEDAC members reported no conflicts of interest related to this submission.

About this Document:

CEDAC provides formulary listing recommendations to publicly funded drug plans. Both a technical recommendation and plain language version of the recommendation are posted on the CADTH website when available.

CDR clinical and pharmacoeconomic reviews are based on published and unpublished information available up to the time that CEDAC made its recommendation.

The manufacturer has reviewed this document and has requested the removal of confidential information in conformity with the *CDR Confidentiality Guidelines*.

The CEDAC Recommendation neither takes the place of a medical professional providing care to a particular patient nor is it intended to replace professional advice.

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Common Drug Review