CEDAC FINAL RECOMMENDATION

LOTEPREDNOL ETABONATE 0.5% OPHTHALMIC SUSPENSION
(Lotemax – Bausch & Lomb)
Indication: Post-operative Inflammation following Cataract Surgery

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

Reason for the Recommendation:
There was insufficient randomized controlled trial evidence comparing loteprednol with other corticosteroid eye drops and, at the confidential price submitted, loteprednol costs more than other corticosteroid eye drops containing dexamethasone and prednisolone.

Of Note:
The Committee noted that given the range of treatment options available for the management of post-operative inflammation following cataract surgery, the quality of evidence comparing loteprednol with other corticosteroid eye drops was low. One published randomized controlled trial (RCT) comparing loteprednol with prednisolone was a small trial with inadequate power to detect clinically meaningful differences and it used a longer duration of treatment than recommended by Health Canada. Two additional trials comparing loteprednol with either fluorometholone or prednisolone were available only as abstracts, with insufficient details provided for their appraisal. The manufacturer was unable to provide additional information on these studies, despite a request for such information.

Background:
Loteprednol is a corticosteroid with a Health Canada indication for the treatment of post-operative inflammation following cataract surgery.

Loteprednol 0.5% is available as an ophthalmic suspension in 5 mL and 10 mL bottles. The Health Canada-recommended dose of loteprednol is one to two drops four times daily into the operated eye beginning 24 hours after cataract surgery and continuing throughout the first two weeks of the post-operative period.

Summary of CEDAC Considerations:
The Committee considered the following information prepared by the Common Drug Review (CDR): a systematic review of RCTs and a critique of the manufacturer's pharmacoeconomic evaluation. The manufacturer submitted a confidential price for loteprednol. Only published trials that included a corticosteroid as an active comparator were included in the CDR systematic review, as it is established that compared with placebo, corticosteroids are effective in the prevention and management of ocular inflammation.

Clinical Trials
The CDR systematic review included one double-blind RCT in 40 patients (40 eyes), the Karalezli study, comparing loteprednol with prednisolone in adult patients who underwent uncomplicated cataract removal surgery.

The Karalezli study had a number of limitations; therefore, firm conclusions could not be drawn based on this study and the Committee did not focus on it. Limitations of the trial included: evaluating four weeks of treatment rather than the Health Canada-recommended treatment duration of two weeks, reporting outcomes at only one and four weeks following treatment, the primary outcome was not specified, insufficient description of blinding methods, and inadequate power to detect clinically meaningful differences.

The Committee considered other studies evaluating loteprednol for the management of post-operative inflammation following cataract surgery that did not meet the systematic review protocol but were summarized in the CDR review. These included two placebo-controlled trials evaluating loteprednol at the Health Canada-approved dose and treatment duration; one RCT comparing loteprednol with a non-steroidal anti-inflammatory drug, ketorolac; and two RCTs comparing loteprednol with either fluorometholone or prednisolone that were available only as abstracts. Overall, the evidence comparing loteprednol with other corticosteroids was limited.

Cost and Cost-Effectiveness
The manufacturer submitted a cost-effectiveness analysis comparing loteprednol with prednisolone, dexamethasone, and fluorometholone for post-operative inflammation in patients who underwent cataract surgery. Given the poor quality of clinical evidence for loteprednol, the Committee focused on the cost of loteprednol and comparators.

The confidential price submitted for loteprednol was $[redacted] per 5 mL bottle, which is more costly than dexamethasone ($7.70 per 5 mL) and prednisolone ($9.70 per 5 mL), and similar in cost to fluorometholone ($12.74 per 5 mL).

Other Discussion Points:
- The Committee considered that there is insufficient evidence to support the manufacturer's claim that loteprednol is associated with less of an increase in intraocular pressure compared with other corticosteroid eye drops used in the management of inflammation following cataract surgery.
- Consistent with the premise of the CDR systematic review, two double-blind, randomized, placebo-controlled trials, LE-125 and LE-127, have demonstrated that loteprednol is

statistically significantly better than placebo in the management of ocular inflammation. In these two placebo-controlled trials that evaluated loteprednol for two weeks using the Health Canada-approved dose, statistically significantly more patients in the loteprednol group compared with the placebo group achieved resolution of inflammation (64% versus 29% in LE-125 and 55% versus 28% in LE-127).

Canadian Expert Drug Advisory Committee (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, and Dr. Yvonne Shevchuk.

Regrets:
Dr. Doug Coyle and Dr. Kelly Zarnke.

Conflicts of Interest:
One CEDAC member reported a conflict of interest and did not participate in the vote.

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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