



CDEC FINAL RECOMMENDATION

MOMETASONE FUROATE

(Asmanex – Merck Canada Inc.)

Indication: Asthma, (Bronchial) Prophylactic Management of Steroid-Responsive

Recommendation:

The Canadian Drug Expert Committee (CDEC) recommends that mometasone furoate be listed for the prophylactic management of steroid-responsive bronchial asthma.

Reasons for the Recommendation:

1. Based on a systematic review including six randomized controlled trials (RCTs), mometasone demonstrated similar or greater efficacy compared with other available inhaled corticosteroids, based on improvements in lung function tests and symptom scores, and reductions in rescue medication use.
2. The daily cost of mometasone is similar to other available inhaled corticosteroids.

Background:

Mometasone furoate has a Health Canada indication for the prophylactic management of steroid-responsive bronchial asthma in patients 12 years of age or older. Mometasone is a corticosteroid with anti-inflammatory properties, and is administered by oral inhalation through a compact breath-actuated dry powder inhaler device. The Health Canada-approved product monograph states that the usual recommended dose is 400 mcg once daily by oral inhalation. The maximum daily recommended dose is 400 mcg twice daily.

Summary of CDEC Considerations:

The Committee considered the following information prepared by the Common Drug Review (CDR): a systematic review of RCTs of mometasone furoate, a critique of the manufacturer's pharmacoeconomic evaluation, and patient group-submitted information about outcomes and issues important to patients.

Clinical Trials

The systematic review included six RCTs comparing mometasone furoate with fluticasone propionate (one trial), budesonide (two trials), and beclomethasone dipropionate (three trials) in patients 12 years and older with asthma.

Common Drug Review

- Study I96-111 (N = 733) was an evaluator-blinded RCT with patients assigned to one of four treatment groups: mometasone furoate (100 mcg, 200 mcg, or 400 mcg), or fluticasone propionate 250 mcg; all twice daily for 12 weeks.
- Study I96-112 (N = 730) was an evaluator-blinded RCT with patients assigned to one of four treatment groups: mometasone furoate (100 mcg, 200 mcg, or 400 mcg) or budesonide 400 mcg; all twice daily for 12 weeks.
- Study C96-134 (N = 365) was a double-blind RCT with patients assigned to one of five treatment groups: mometasone furoate (100 mcg, 200 mcg, or 400 mcg), beclomethasone dipropionate 168 mcg, or placebo; all twice daily for 12 weeks.
- Study C96-135 (N = 239) was an evaluator-blinded RCT with patients assigned to one of four treatment groups: mometasone furoate 200 mcg or 400 mcg twice daily, mometasone furoate 800 mcg once daily, or beclomethasone dipropionate 168 mcg twice daily, for 52 weeks.
- Study C96-168 (N = 227) was a double-blind RCT with patients assigned to one of four treatment groups: mometasone furoate (100 mcg or 200 mcg), beclomethasone dipropionate 168 mcg, or placebo; all twice daily for 12 weeks.
- The Corren study (N = 262) was a double-blind RCT with patients assigned to one of three treatment groups: mometasone furoate 440 mcg, budesonide 400 mcg, or placebo; all once daily for eight weeks.

All studies included a one- to two-week run-in period during which patients continued the use of their previously prescribed inhaled corticosteroids, and baseline pulmonary function was measured by spirometry. After entering the treatment period, previously used oral and inhaled corticosteroids were discontinued, while rescue medications such as inhaled salbutamol were permitted. In addition, theophylline was allowed throughout the study if it had been used at a stable dose before screening.

The percentage of patients completing the trial ranged from 79% to 90% across active-treatment groups, with the exception of the 52-week study (C96-135) in which completion ranged from 72% to 86% across treatment groups. Limitations of the studies include the different delivery devices used for the inhaled corticosteroids, and that trials were designed as superiority trials; the trials did not pre-declare a non-inferiority margin and therefore the trials could not be analyzed as non-inferiority trials.

Outcomes

Outcomes were defined a priori in the CDR systematic review protocol. Of these, the Committee discussed the following: change in baseline lung function, asthma symptoms, acute asthma exacerbations, rescue medication use, and nocturnal awakenings. Adverse events, including serious adverse events and withdrawal due to adverse events, were also discussed.

The primary outcome in all studies (with the exception of study C96-135) was the change from baseline in lung function, as measured by the forced expiratory volume in one second (FEV₁). The primary outcome in study C96-135 was the incidence of adverse events. None of the included trials reported between-treatment comparisons in asthma exacerbation frequency, exacerbation-related health care utilization, or quality of life.

Results

Efficacy or Effectiveness

The Committee focused its discussion on the mometasone 200 mcg or 400 mcg twice daily treatment groups in comparison with other inhaled corticosteroids.

- FEV₁ increased from baseline to end point by 0.15 L to 0.28 L in patients randomized to mometasone 200 mcg or 400 mcg. The change from baseline to end point in FEV₁ was not statistically significantly different for mometasone compared with fluticasone or beclomethasone. However, the increase in FEV₁ was statistically significantly greater for mometasone compared with budesonide; mean difference (MD) (95% confidence interval [CI]), 0.1 L (0.02 to 0.18) for both 200 mcg and 400 mcg of mometasone.
- Change from baseline in peak expiratory flow rate was not statistically significantly different in patients randomized to mometasone compared with other inhaled corticosteroids.
- Use of rescue medication (inhaled salbutamol) was not statistically significantly different in patients randomized to mometasone compared with fluticasone or beclomethasone. In study I96-112, the mean change from baseline in the daily salbutamol dose was statistically significantly greater for patients randomized to mometasone 200 mcg, compared with budesonide 400 mcg; -91 mcg versus -34 mcg, respectively.
- Change from baseline to end point in symptom scores for each of the three categories of “wheezing”, “difficult breathing”, and “coughing” were similar across the studies and were not notably different between active treatment groups.
- The change in the number of nocturnal awakenings was not statistically significantly different for patients randomized to mometasone compared with other inhaled corticosteroids.

Harms (Safety and Tolerability)

Harms data were available from five studies; the Corren study did not provide data on adverse events.

- The incidence of serious adverse events was similar between mometasone and other active treatments in the trials providing data. Serious adverse events were most commonly observed in the 52-week study (C96-135); 20% to 37% in the mometasone groups, compared with 38% in the beclomethasone group.
- The incidence of adverse events, and withdrawal due to adverse events, was similar between active treatment groups in all studies providing data. The most common adverse events, reported by ≥ 10% of patients in any treatment group in both study I96-111 and study I96-112, included: headache, pharyngitis, viral infection, and rhinitis. The most common adverse events in studies C96-134, C96-168, and C96-135 were respiratory system disorders, headache, oral candidiasis, musculoskeletal pain, back pain, viral infection, and dysmenorrhea.

Cost and Cost-Effectiveness

The manufacturer submitted a cost-comparison analysis of mometasone with four other inhaled corticosteroid therapies (beclomethasone dipropionate, budesonide, ciclesonide, and fluticasone propionate). The justification for conducting a cost-comparison analysis was based on the findings from head-to-head active comparator RCTs demonstrating similar efficacy and safety between mometasone furoate and other inhaled corticosteroid therapies.

The daily cost of mometasone furoate (\$0.58 to \$2.33) is similar in price when compared with beclomethasone (\$0.75 to \$2.39), budesonide (\$0.63 to \$3.38), ciclesonide (\$0.36 to \$2.40), and fluticasone (\$0.80 to \$2.75).

Patient Input Information:

The following is a summary of information provided by one patient group that responded to the CDR Call for Patient Input:

- It was noted that uncontrolled asthma negatively affects quality of life due to a reduction in physical exercise, an inactive social life, missed work and school, night awakenings, and hospital or emergency room visits.
- Of prime importance to patients with asthma is the ability to maintain or improve lung function, and to reduce the frequency and severity of exacerbations and night-time awakenings.
- No patients reported experience with mometasone, however, patients expressed the desire to have additional options for controller medications, noting that many patients try numerous controller medications before they find one that is both effective and has minimal side-effects.

Other Discussion Points:

- The Committee discussed the fact that no mometasone safety data are available from RCTs longer than one year in duration. However, the Committee noted that mometasone furoate has been in use for the treatment of asthma in numerous countries since 2003.
- The Committee noted that the reviewed trials provided no evidence for the benefit of once daily dosing of mometasone 400 mcg compared with twice daily dosing of fluticasone, budesonide, or beclomethasone.
- The Committee noted that patents for fluticasone are expected to expire in 2012.

CDEC Members:

Dr. Robert Peterson (Chair), Dr. Lindsay Nicolle (Vice-Chair), Dr. Ahmed Bayoumi, Dr. Bruce Carleton, Ms. Cate Dobhran, Mr. Frank Gavin, Dr. John Hawboldt, Dr. Peter Jamieson, Dr. Julia Lowe, Dr. Kerry Mansell, Dr. Irvin Mayers, Dr. Yvonne Shevchuk, Dr. James Silvius, and Dr. Adil Virani.

April 18, 2012 Meeting

Regrets:

One CDEC member did not attend.

Conflicts of Interest:

None

About this Document:

CDEC 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.

Common Drug Review

CDR clinical and pharmacoeconomic reviews are based on published and unpublished information available up to the time that CDEC made its recommendation. Patient information submitted by Canadian patient groups is included in the CDR reviews and used in the CDEC deliberations.

The manufacturer has reviewed this document and has not requested the removal of confidential information in conformity with the *CDR Confidentiality Guidelines*.

The Final CDEC 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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