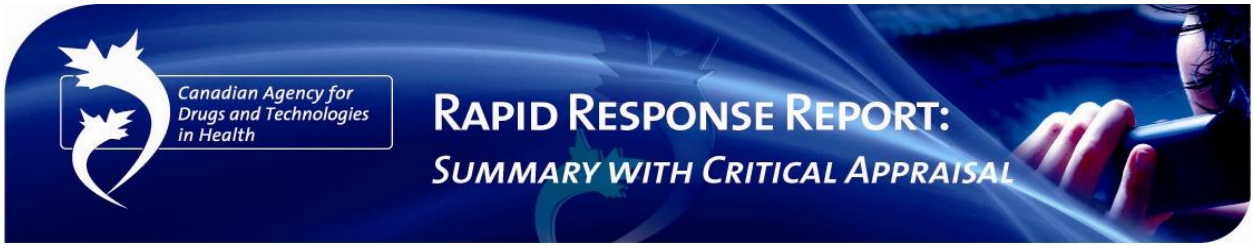

TITLE: Fluticasone Furoate versus Fluticasone Propionate for Seasonal Allergic Rhinitis: A Review of the Clinical and Cost-Effectiveness

DATE: 13 June 2011

CONTEXT AND POLICY ISSUES:

Seasonal allergic rhinitis is a common disorder with an US prevalence of about 10-30% in adults and 40% in children, affecting close to 60 million people.[1,2] The Canadian Allergy, Asthma and Immunology Foundation estimates that 20-25% of Canadians have allergic rhinitis.[3] In addition to allergen avoidance and immunotherapy, antihistamines and corticosteroids nasal spray are used to control nasal and ocular symptoms.[4,5]

Fluticasone furoate nasal spray (Avamys™ by GlaxoSmythKline Inc.) was approved by Health Canada in August 2007 for the treatment of seasonal allergic rhinitis.[6] The efficacy of fluticasone furoate nasal spray for the treatment of nasal and ocular symptoms of allergic rhinitis was shown in a recent systematic review,[7] as well as in randomized, double-blind, placebo-controlled studies.[8,9] Fluticasone furoate nasal spray was not associated with hypothalamic-pituitary-adrenal axis suppression as shown in a randomized, double blind, placebo- and active-controlled (prednisone) study.[10]

To help in the consideration of formulary coverage of fluticasone furoate (Avamys™) for seasonal allergic rhinitis, this report compares the clinical and cost-effectiveness of fluticasone furoate with fluticasone propionate for the treatment of seasonal allergic rhinitis.

RESEARCH QUESTIONS:

1) What is the clinical effectiveness of fluticasone furoate for seasonal allergic rhinitis as compared to fluticasone propionate?

2) What is the cost-effectiveness of fluticasone furoate for seasonal allergic rhinitis as compared to fluticasone propionate?

KEY MESSAGE:

Two randomized controlled studies showed similar efficacy between fluticasone propionate and fluticasone furoate in the management of symptoms of seasonal allergic rhinitis; no evidence on the cost-effectiveness of fluticasone furoate as compared with fluticasone propionate was identified.

METHODS:

Literature search strategy

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2011, Issue 5), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials and economic studies. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2006 and May 17, 2011.

Selection criteria and method

One reviewer screened the titles and abstracts of the retrieved publications and examined the full-text publications for the final article selection. Selection criteria are outlined in Table 1.

Table 1: Selection Criteria

Population	Adults 18 years and older with seasonal allergic rhinitis
Intervention	Fluticasone furoate (Avamys)
Comparator	Fluticasone propionate
Outcomes	Symptoms including runny nose, blocked nose, itching and sneezing or symptoms that affect the eyes, such as irritation, watering or redness Economic outcomes
Study designs	Health technology assessment, systematic reviews, meta-analyses, randomized controlled trials, and economic evaluations

Exclusion criteria

Articles were excluded if they did not meet the selection criteria in table 1, if they were published before 2006, or if they were duplicate publications of the same study.

Critical appraisal of individual studies

The quality of the included studies was assessed using the SIGN 50 check list.[11]

SUMMARY OF EVIDENCE:

Quantity of research available

One hundred and nine studies were identified from the literature search, and ten additional studies were identified by searching the grey literature. From these, 12 potentially relevant studies were selected for full-text screening, and two clinical trials were selected for inclusion. Appendix 1 describes the PRISMA flowchart of the included studies.

Summary of study characteristics

The characteristics of the included study are summarized in Table 2.

Table 2: Characteristics of Included Studies

First Author, Publication Year, Country	Study Design, Length of Follow-up	Patient Characteristics, Sample Size	Intervention	Comparators	Clinical Outcomes
Okubo, 2009, Japan[12]	RCT, double-blind. Two-week treatment. One week post-treatment follow-up	Adult patients with Japanese cedar pollinosis, n = 446 patients	Fluticasone furoate	Fluticasone propionate; placebo	Sneezing, rhinorrhea, nasal congestion
Meltzer, 2010, US[13]	RCT, double-blind. Two- week cross over treatment. Three to five days post-treatment follow-up	Adult patients with allergic rhinitis, n = 360 patients	Fluticasone furoate	Fluticasone propionate; placebo	Sneezing, rhinorrhea, nasal congestion, nasal itching. Adverse events. Product sensory attributes*

*Product sensory attributes: odor, after taste, drip down the throat, nose runoff
RCT= randomized controlled trial

Summary of critical appraisal

The included studies adequately addressed the research questions**.** Patients randomization and drop-outs were reported adequately. Allocation concealment was not indicated in one study, and was adequate in the other. Because of the physical discrepancy between the two types of nasal sprays, complete blinding was not possible. The study by Meltzer[13] was a crossover study, and there was no direct comparison between the two treatments.

Table 3: Summary of Critical Appraisal of Included Randomized Controlled Trials

First Author	Concealment of Randomization	Trial Stopped Early	Type of Blinding	Loss to Follow-up in Each Trial Arm
Okubo[12]	Not reported	No	Double blind	No
Meltzer[13]	Adequate	No	Double blind	1 patient (<1%)

Summary of findings

Clinical effectiveness of fluticasone furoate for seasonal allergic rhinitis as compared with fluticasone propionate

The literature search identified two double-blind, randomized controlled trials comparing fluticasone furoate to fluticasone propionate for the treatment of seasonal allergic rhinitis.[12,13]

Okubo et al[12] compared the efficacy and safety of fluticasone furoate nasal spray 110 µg once daily, with fluticasone propionate nasal spray 100 µg twice daily, and to placebo, in 446 adult patients with Japanese cedar pollinosis. Patients were asked to use an allergy diary. The main efficacy end points were the mean change from baseline of three individual symptom scores for sneezing, rhinorrhea, and nasal congestion (scores of 0 to 9), and the number of days until onset of action. The incidence of adverse events between the two groups was also reported. The mean change from baseline in nasal symptoms over the two-week treatment period was similar in the fluticasone furoate and fluticasone propionate groups [-1.23 (standard error 0.14) and -1.06 (standard error 0.14) respectively]. The reduction in symptoms against placebo was observed from the first day of treatment in the fluticasone furoate group, while it was observed from the second day of treatment in the fluticasone propionate group. The incidence of adverse events was 17% in the fluticasone furoate group, and 18% in the fluticasone propionate group (p values not reported).

Meltzer et al[13] compared the efficacy and patient preference of fluticasone furoate nasal spray, 110 µg once daily, with fluticasone propionate nasal spray 200 µg once daily, and with placebo, in 360 adult patients with seasonal allergic rhinitis. Patients were asked to use an allergy diary. The main efficacy end points were the mean change from baseline of four individual symptom scores for sneezing, rhinorrhea, nasal congestion, and nasal itching (scores of 0 to 12), and patient preference. Fluticasone furoate and fluticasone propionate had similar symptom reduction (p value not reported). Compared to placebo, both drugs had statistically significantly better symptom reduction [-0.8 (standard deviation 0.24), $p < 0.001$ and -0.6 (standard deviation 0.24), $p = 0.01$, respectively]. Based on preference of scent or odor, 58% of patients preferred fluticasone furoate while 27% preferred fluticasone propionate. Similarly, patients favored fluticasone furoate when considering medication leaking out of the nose or down the throat (59% vs 21%), the aftertaste (60% vs 18%), and the gentleness of the mist (57% vs 26%). Adverse events occurred in 12% of patients with fluticasone furoate and in 21% of those with fluticasone propionate. Headache, the most commonly reported adverse event, occurred in 4% of patients with fluticasone furoate and 9% of those with fluticasone propionate (p values not reported). Most events were described as mild or moderate.

Cost-effectiveness of fluticasone furoate for seasonal allergic rhinitis as compared to fluticasone propionate

The literature search did not identify economic studies that compared the cost-effectiveness of fluticasone furoate with fluticasone propionate

Limitations

The literature search identified two studies comparing the clinical efficacy of fluticasone furoate nasal spray with fluticasone propionate nasal spray. The sample sizes included 360 patients and 446 patients. The studies are limited by the fact that there were physical discrepancies between the two types of nasal sprays which affected blinding. One of the studies used a crossover design with no wash-out period between the two treatment periods. Finally, the study duration was two weeks and the effectiveness of these products when used for prolonged period of times is unknown.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING:

The evidence comparing the clinical effectiveness of fluticasone furoate nasal spray to fluticasone propionate nasal spray in the treatment of seasonal allergic rhinitis is limited. Data found that both drugs have similar clinical efficacy in reducing nasal and ocular symptoms, with fluticasone furoate nasal spray being preferred to fluticasone propionate nasal spray based on sensory attributes. Findings on adverse events were inconsistent, with adverse event rates similar between the two drugs in one study, and favouring fluticasone furoate in another.

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APPENDICES:

APPENDIX 1: Selection of Included Studies