# DRAFT

## Oregon Health Resources Commission

# Inhaled Corticosteroid (ICS)
## Update Report

**Update Report #1**
**January 2006**

**This report is the first update of the initial ICS Subcommittee Report of April 2005. All revisions are highlighted.**

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## *Overview*

The 2001 session of the Oregon Legislature passed Senate Bill 819, authorizing the creation of a Practitioner-managed Prescription Drug Plan (PMPDP). The statute specifically directs the Health Resources Commission to advise the Department of Human Services on this Plan.

In the winter of 2004 the Oregon Health Resources Commission (HRC) appointed a subcommittee to perform an evidence-based review of the use of Inhaled Corticosteroids (ICS) drugs. Members of the subcommittee consisted of physicians, a pharmacist, a PharmD, a Pediatric Nurse Practitioner, and other health care professionals. The subcommittee had four meetings. All meetings were held in public with appropriate notice provided.

Subcommittee members worked with the Center for Evidence-based Policy (Center) and the Oregon Health and Science University's (OHSU) Evidence-based Practice Center (EPC) to develop and finalize key questions for drug class review, specifying patient populations, medications to be studied and outcome measures for analysis, considering both effectiveness and safety. Evidence was specifically sought for subgroups of patients based on race, ethnicity and age, demographics, other medications and co-morbidities.

The OHSU EPC subcontracted with University of North Carolina at Chapel Hill (RTI-UNC) EPC for this drug class. Using standardized methods, the RTI-UNC Evidence-based Practice Center reviewed systematic databases, the medical literature and dossiers submitted by pharmaceutical manufacturers. Inclusion and exclusion criteria were applied to titles and abstracts, and each study was assessed for quality according to predetermined criteria. The RTI-UNC EPC's report, "Drug Class Review on Inhaled Corticosteroids" was completed in January 2005, circulated to subcommittee members and posted on the web. The subcommittee met on February 24, 2005 to review the document and by consensus agreed to adopt the EPC report. Time was allotted for public comment, questions and testimony.

The OHSU-EPC's updated final report update #1, "*Drug Class Review on Inhaled Corticosteriods"* was completed January 2006, circulated to the Standing Update Committee members and posted on the OHPR website at http://www.oregon.gov/DAS/OHPPR/ORRX/HRC/evidence_based_reports.shtml. The Standing Update Committee met on January 10, 2006 and February 7, 2006 to review the document and write this report. By consensus, the committee members agreed to adopt the EPC report. Time was allotted for public comment, questions and testimony. All available sources of information from the EPC's report that included information submitted by pharmaceutical manufacturers and public testimony, were considered. The Standing Update Committee presented its findings to the HRC and the revisions were approved at its meeting on _____.

This report does not recite or characterize all the evidence that was discussed by the RTI-UNC EPC, the ICS Subcommittee, or the Health Resources Commission. This report is not a substitute for any of the information provided during the subcommittee process, and readers are encouraged to review the source materials. This report is prepared to facilitate

the Health Resources Commission in providing recommendations to the Department of Human Services.

The Standing Update Committee of the Health Resources Commission, working together with the EPCs, Center, OMAP, and the Oregon State University College of Pharmacy, will monitor medical evidence for new developments in this drug class. At least once per year new pharmaceuticals will be reviewed and if appropriate, a recommendation for inclusion in the PMPDP will be made. For pharmaceuticals on the plan, significant new evidence will be assessed and Food and Drug Administration changes in indications and safety recommendations will be evaluated. The ICS report will be updated as indicated by the Standing Update Subcommittee. Substantive changes will be brought to the attention of the Health Resources Commission, who may choose to approve the report, or reconvene an ICS Subcommittee.

The full RTI-UNC EPC's draft report, *Drug Class Review on Inhaled Corticosteroid,* is available on the Office for Oregon Health Policy & Research, Practitioner-Managed Prescription Drug Plan website: www.oregonrx.org. Information regarding the Oregon Health Resources Commission and its subcommittee policy and process can be found on the Office for Oregon Health Policy & Research website: http://www.oregon.gov/DAS/OHPPR/ORRX/HRC/evidence_based_reports.shtml
You may request more information including copies of the draft report, minutes and tapes of subcommittee meetings, from:

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Information dossiers submitted by pharmaceutical manufacturers are available upon request from the OHSU Center by contacting:

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There will be a charge for copying and handling in providing documents both from the Office of Oregon Health Policy & Research and from the Center.

# Drug Class Review for Inhaled Corticosteroids

Asthma and chronic obstructive pulmonary disease (COPD) differ in pathogenesis and therapeutic response and should be considered different disease entities even though they might co-exist in some individuals. Asthma is characterized by episodic reversible airflow obstruction that has an inflammatory component.[1] COPD airflow limitation is usually progressive, irreversible, and associated with an abnormal inflammatory response to noxious particles or gases, primarily from smoking.[2] In the US more that 7% of adults and 12% of children are affected by asthma. In 2000, asthma accounted for 10.4 million outpatient visits, 1.8 million visits to the emergency department, 500,000 hospitalizations, and 4,487 deaths.[3] Although COPD prevalence is lower than asthma at 5.5%, it accounts for a larger portion of health care utilization due to its higher morbidity and mortality. In 2000, COPD accounted for 20.7 million outpatient visits, 3.4 million visits to the emergency department, 6.3 million hospitalizations, and 116,513 deaths.[4]

Because asthma and COPD have a different pathogenesis and therapeutic response, treatment guidelines differ for the two. Current treatment guidelines for asthma suggest that daily long-term control medications are necessary to prevent exacerbations and chronic symptoms. Inhaled corticosteroids (ICSs) are preferred because of their ability to control the underlying inflammatory processes. Leukotriene inhibitors/receptor blockers are alternative anti-inflammatory medications, but are less effective than inhaled steroids.[5]

Although the FDA has not approved ICSs as monotherapy for the treatment of COPD, ICSs are believed to improve some clinical outcomes.[6] A recent review suggests that inhaled combinations of long-acting $\beta_2$–agonists and corticosteroids are slightly more efficacious than either inhalant alone.[7] ICSs are favored over oral corticosteroids because their anti-inflammatory effect is directed at the airways, which reduces the risk of unwanted systemic side effects. The five different ICSs currently available in the US are summarized in Table 1.

Product formulation and delivery devices vary among products; ICSs can be delivered via nebulization, pressurized metered dose inhaler (MDI), or dry power inhaler (DPI). ICS products differ in their pharmacokinetic and pharmacodynamic properties as well as in characteristics of the delivery device. The use of spacers can alter the amount of drug deposited per actuation. Although clinical comparative trials suggest six-fold differences in potencies among the available products, one review article concludes that currently no

[1] National Asthma Education and Prevention Program. Expert Panel Report 2:Guidelines for the Diagnosis and Management of Asthma – 1997.
[2] www.thoracic.org/copd/. American Thoracic Society
[3] www.cdc.gov/nchs/data/factsheets/asthma.pdf. National Center for Health Statistics
[4] www.cdc.gov/nchs/data/factsheets/copd.pdf National Center for Health Statistics
[5] Sin DD, Man J, Sharpe H, et al. Pharmacological management to reduce exacerbations in adults with asthma: a systematic review and metaanalysis. *JAMA* 2004; 292:367-76.
[6] www.thoracic.org/copd/
[7] Sin DD, McAlister FA, Man SF, et al. Contemporary management of chronic obstructive pulmonary disease: scientific review. *JAMA* 2003; 290:2301-12.

evidence supports differences in efficacy when these drugs are administered at equipotent doses.[8] Some believe, however, safety and tolerability may differ when used at equipotent doses. In addition, product formulation lead to dramatic differences in the number of actuations required to deliver equipotent doses, and this may affect patient adherence. No single study is sufficient to provide the information required to make clinical decisions about the superiority of one ICS over another.[9] Because potencies and delivery vary between ICSs, it is difficult to compare clinically equivalent drug, dose, and device combinations. The RTI-UNC Evidence-based practice center used comparative dosing parameters from the National Asthma Education and Prevention Program (NAEPP) Expert Panel Report[10] and the International Primary Care Airways Group (IPAG) Diagnosis and Management Handbook[11].
Table 1 summarizes the six different ICSs.

## Table 1. Inhaled corticosteroid trade names, manufacturers, formulations, adult maximal activations per day, and labeled uses.

| Generic Name | US Trade Name | Manufacturer | Dosage Form/Device | Strength | High Dose Adult | Labeled Uses |
|---|---|---|---|---|---|---|
| **Beclomethasone dipropionate** | QVAR® | Ivax/3M | MDI (HFA) | 40 mcg/puff<br>80 mcg/puff | >12 puffs/day<br>> 6 puffs/day | Asthma (≥5yrs) |
| | Vanceril® | Schering-Plough | MDI (CFC) | 42 mcg/puff<br>84 mcg/puff | >20 puffs/day<br>>10 puffs/day | Asthma (≥5yrs) |
| **Budesonide** | Pulmicort Turbohaler® | AstraZeneca | DPI | 200 mcg/dose | > 6 puffs/day | Asthma (≥6yrs) |
| | Pulmicort Respules® | AstraZeneca | Inhalation Suspension | 500 mcg<br>1000 mcg<br>2000 mcg | | Asthma (Age 1-8) |
| **Flunisolide** | Aerobid®<br>Aerobid®-M | Forest/3M | MDI (CFC) | 250 mcg/puff | > 8 puffs/day | Asthma (≥6yrs) |
| | Bronalide | Boehringer Ingelhelm (Canada) | MDI (CFC) | 44 mcg/puff | | Asthma (≥4yrs) |
| **Fluticasone** | Flovent® | GlaxoSmithKline | MDI (CFC) | 44 mcg/puff<br>110 mcg/puff<br>220 mcg/puff | >15 puffs/day<br>> 6 puffs/day<br>> 3 puffs/day | Asthma (≥4yrs) |
| | Flovent®Discus | GlaxoSmithKline | DPI-breath activated | 50 mcg/puff<br>100 mcg/puff<br>250 mcg/puff | >12 puffs/day<br>> 6 puffs/day<br>> 2 puffs/day | Asthma (≥4yrs) |
| **Mometasone** | Asmanex® Twisthaler | Schering-Plough | DPI | 220 mcg/puff | > 2 puffs/day | Asthma (>12yrs) |
| **Triamcinolone** | Azmacort® | Aventis | MDI (CFC) w/ spacer | 100 mcg/puff | >20 puffs/day | Asthma (≥6yrs) |

[8] Kelly HW. Pharmaceutical characteristics that influence the clinical efficacy of inhaled corticosteroids. *Ann Allergy Asthma Immunol.* 2003; 91:362-34; quiz 334-5, 404.
[9] O'Byrne PM, Pedersen S. Measuring efficacy and safety of different inhaled corticosteroid preparations. *J. Allergy Asthma Immunol* 1998; 102;879-86.
[10] National Asthma Education and Prevention Program. Expert Panel Report: Guidelines for the Diagnosis and Management of Asthma Update on Selected Topics-2002. J. Allergy Clin Imunol 2002;110(5 Suppl):S141-219.
[11] International Primary Care Airways Group (IPAG). IPAG Diagnosis & Management Handbook. Chronic Airways Disease A Guide for Primary Care Physicians. 2005

## *Critical Policy:*

*Senate Bill 819*

> "The Department of Human Services shall adopt a Practitioner-managed Prescription Drug Plan for the Oregon Health Plan. The purpose of the plan is to ensure that enrollees of the Oregon Health Plan receive the most effective prescription drug available at the best possible price."

*Health Resources Commission Policy*

1. "Clinical outcomes are the most important indicators of comparative effectiveness"
2. "If evidence is insufficient to answer a question, neither a positive nor a negative association can be assumed."

## *Quality of the Evidence:*

For quality of evidence the ICS subcommittee took into account the number of studies, the total number of patients in each study, the length of the study period, and the end points of the studies. Statistical significance was an important consideration. The subcommittee utilized the EPC's ratings of "good, fair or poor" for grading the body of evidence. Overall quality ratings for an individual study were based on the internal and external validity of the trial.

Internal validity of each trial was based on:

1. Methods used for randomization
2. Allocation concealment and blinding
3. Similarity of compared groups at baseline and maintenance of comparable groups.
4. Adequate reporting of dropouts, attrition, and crossover
5. Loss to follow-up
6. Use of intention-to-treat analysis

External validity of trials was assessed based on:

1. Adequate description of the study population
2. Similarity of patients to other populations to whom the intervention would be applied
3. Control group receiving comparable treatment
4. Funding source that might affect publication bias.

## *Weighing the Evidence*

A particular randomized trial might receive two different ratings: one for efficacy and another for adverse events. The overall strength of evidence for a particular key question reflects the quality, consistency and power of the body of evidence relevant to that question. The subcommittee's task was to identify ICSs that would offer the greatest likelihood of success for the treatment of asthma and COPD.

# Summary of Results

**Key Question 1** For outpatients with asthma or chronic obstructive pulmonary disease (COPD), do inhaled corticosteroids (ICS) differ in effectiveness?

**Asthma**

Twenty-four head-to-head trials and one systematic review[12] compared the efficacy of one ICS to another. Twelve placebo-controlled trials provided further evidence on health outcomes not evaluated in head-to-head trials. No effectiveness trials were available for review.

Overall, head-to-head trials provided fair evidence that ICSs, at equipotent doses administered through comparable delivery devices, do not differ in their ability to control asthma symptoms and reduce the need for rescue medication. In several fair-quality studies comparing fluticasone to another ICS (beclomethasone, budesonide, triamcinolone, and mometasone), fluticasone was superior to the comparator for one or more mixed outcome measures. However some of the studies favoring fluticasone did not compare equipotent doses and this finding was not substantiated by a good-quality systematic review that compared the pooled effect of beclomethasone and budesonide to fluticasone and found no differences in symptom control, β-agonist use, and asthma exacerbations.

Although both studies comparing budesonide with mometasone found better outcomes among mometasone-treated patients, differences again were related to nonequivalent doses thus were not significant. Similarly, dose-related differences were observed favoring fluticasone in the only trial comparing fluticasone with mometasone, although the lower mometasone doses used in this trial are not FDA approved.

In terms of health outcomes, evidence comparing one ICS to another is poor-quality. In three of four head-to-head trials, fluticasone was superior to beclomethasone, budesonide, and triamcinolone in quality of life, disruptions in physical activity, and work absences. However, two of three trials did not compare equipotent doses. A review of 12 placebo-controlled trials (included to evaluate health outcomes not reported in head-to-head trials) provided fair evidence that beclomethasone, budesonide, fluticasone, and mometasone improve quality of life and/or functional status.

**COPD**

No head-to-head trials comparing one ICS to another in COPD were identified. Nine placebo-controlled trials, one high-quality prospective cohort study, and three meta-analyses evaluated the efficacy of an individual ICS or ICS class as a whole primarily in smokers or former smokers with a clinical diagnosis of COPD. However, significant

[12] Adams N, Bestall JM, Jones PW. Fluticasone versus beclomethasone or budesonide for chronic asthma (Cochrane Review). The Cochrane Library 2004;1.

differences in study characteristics made it difficult to identify differences among treatments overall.

The majority of trials did not report statistically significant differences in $FEV_1$ decline, an intermediate outcome, between ICSs and placebo. Two meta-analyses found a modest but statistically significant difference in $FEV_1$ decline with ICS treatment over placebo. Consistent fair to good-evidence exists that ICSs do not reduce overall mortality in patients with COPD. Additionally, the majority of trials did not find significant differences in quality of life between ICSs and placebo. One trial reported that patients with severe COPD experienced a significantly lower decline of quality of life with fluticasone compared to placebo.

**Key Question 1 Consensus**

**The ICS Subcommittee agrees by consensus that for outpatients with asthma:**

- Available evidence does not support a consistent difference in the comparative efficacies of ICSs in their ability to control asthma symptoms, reduce the need for rescue medication, or improve quality of life or functional status.
- There is insufficient evidence to evaluate differences among ICSs for comparative effectiveness.
- It is difficult to extrapolate clinical studies to an entire asthma population because the available evidence fails to consider the number of inhalations required to deliver equivalent doses and/or the patient's ability to comply with treatment.

**The ICS subcommittee agrees by consensus that for outpatients with COPD:**

- In adult outpatients with COPD, there is mixed and poor grade evidence for the effectiveness of ICSs as a class for treatment of $FEV_1$ decline and exacerbation rates.
- There is consistent evidence that ICSs do not reduce mortality or improve quality of life in COPD.
- There is insufficient evidence to evaluate differences among individual ICSs in COPD.

**Key Question 2** For outpatients with asthma or COPD, do inhaled corticosteroids differ in safety or adverse events?

## Local Adverse Effects

Of 19 head-to-head studies reviewed, four reported statistically significant differences in at least one adverse event.[13,14,15,16] two trials reported a significantly higher incidence of sore throat in fluticasone-treated than beclomethasone-treated patients. One study reported significantly more upper respiratory infections in triamcinolone-treated than in beclomethasone-treated patients, and one study reported oral candidiasis in significantly more fluticasone-treated than in triamcinolone-treated patients. One trial compared nonequivalent doses of fluticasone and triamcinolone, with more potent doses of fluticasone associated with a higher incidence of oral candidiasis. Common mild adverse side effects were reported in fewer than 10% of ICS-treated patients and included rhinitis, oral candidiasis, sore throat, hoarseness, headache, cough, and bronchitis. Upper respiratory infections were reported by 3-32% of study participants with the higher frequency noted in the pediatric populations. No trial reported differences in discontinuation rates because of adverse events.

## Bone Density and Osteoporosis

Overall the evidence of an association between ICS products and osteoporosis is mixed. The strongest evidence comes from six studies that measured fractures. Of these six studies, two good-rated case-control studies[17] and a fair-rated retrospective cohort study[18] reported a small dose-dependent increase in the risk of fracture for ICS-treated patients compared to patients that had not been exposed to an ICS. One fair-rated case-control study[19] and two RCTs[20,21] did not support this finding. Although one RCT did not support an increased risk of fracture, this trial did find a greater reduction in BMD among triamcinolone-

[13] Gustafson P, Tsanakas J, Gold M, et al. Comparison of the efficacy and safety of inhaled fluticasone propionate 200 micrograms/day with inhaled beclomethasone dipropionate 400 micrograms/day in mild and moderate asthma. *Arch Dis. Child.* 1993; 69(2):206-11.

[14] Lundback B, Alexander M, Day J et al. Evaluation of fluticasone proprionate (500 micrograms/day) administered either as dry powder via a Diskhaler inhaler or pressurized inhaler and compared with beclomethasone dipropionate (1000 micrograms/day) administered by pressurized inhaler. *Respiratory Med* 1993; 87(8):609-20.

[15] Bronsky E, Korenblat P, Harris AG, et al. Comparative clinical study of inhaled beclomethasone dipropionate and triamcinolone acetonide in persistent asthma. *Ann Allergy Asthma Immunol* 1998; 80(4):295-302

[16] Condemi JJ, Chervinsky P, Goldstein MF et al. Fluticasone propionate powder administered through Diskhaler versus triamcinolone acetonide aerosol administered through metered-dose inhaler in patients with persistent asthma. *J. Allergy Clin Immunol* 1997; 100(4):467-74.

[17] Lee TA, Weiss KB. Fracture risk associated with inhaled corticosteroid use in chronic obstructive pulmonary disease. *Am. J. Respir. Crit. Care Med* 2004; 169(7):855-9.

[18] vanStaa TP, Leukfens HG, Cooper C. Use of inhaled corticosteroids and risk of fractures. J Bone Miner Res 2001;16(3):581-8.

[19] Johannes CB, Schneider GA, Dube TJ, et al. The risk of nonvertebral fracture related to inhaled corticosteroid exposure among adults with chronic respiratory disease. Chest 2005,127*1):89-97.

[20]

[21]

treated patients compared to placebo.[22] Additionally, evidence of an ICS-associated reduction in bone mineral density (BMD) comes from one small prospective cohort study in pre-menopausal women[23]; however, four additional studies suggest no relationship between ICS use and reduction in BMD.

**Growth Rate**

Fair evidence suggests that short-term growth rate is reduced with ICS use. Two small, head-to-head trials provided fair evidence that short-term growth rate is reduced significantly with fluticasone, beclomethasone, and budensonide. In each study, the reduction in growth was statistically greater with beclomethasone[24] and budensonide[25] compared to fluticasone; however the absolute differences were small. A placebo-controlled meta-analysis reported a significant reduction in growth rate for beclomethasone.[26] Most of these studies address only ICS treatment duration up to one year. Furthermore, one long-term observational study did not detect differences in linear growth and adult height between budesonide-treated children with asthma and controls without ICS treatment or their healthy siblings. Insufficient evidence exists to determine whether long-term treatment with ICSs leads to a reduction in adult height.

**Acute Adrenal Crisis**

Evidence from randomized trials and observational studies is insufficient to draw conclusions regarding the risk of rare but potentially fatal adverse events such as acute adrenal crisis.

**Cataracts**

No study compared the risk of developing posterior sub-capsular cataracts (PSC) between one ICS and another. No significant differences between ICS users and controls have been reported for the risk of PSC in children, adolescents, or adults < 40 years of age. In older individuals who took ICSs, there was an increased risk that was dose and duration related. No study evaluated the link between childhood ICS use and risk of cataracts in old age.

**Ocular Hypertension and Open-angle Glaucoma**

[22] Scanlon PD, Coinnett JE, Wise RA, et al. Loss of bone density with inhaled triamcinolone in Lung Health Study II. Am J Respir Crit Care Med 2004;170(12):1302-9.
[23] Israel E, Banerjee TR, Fitzmaurice GM, et al. Effects of inhaled glucocorticoids on bone density in premenopausal women. *NEJM* 2001; 345(13):941-7.
[24] De Benedictis FM, Teper A, Green RJ et al. Effects of 2 inhaled corticosteroids on growth: results of a randomized controlled trial. *Arch Pediatr Adolesc Med* 2001; 155(11):1248-54.
[25] De Benedictis FM, Teper A, Green RJ et al. Effects of 2 inhaled corticosteroids on growth: results of a randomized controlled trial. *Arch Pediatr Adolesc Med* 2001; 155(11):1248-54.
[26] Sharek PJ, Bergman DA, Ducharme F. Beclomethasone for asthma in children: Effects on linear growth (Cochrane Review). *The Cochrane Library* 2004; 1.

No study compared the risk of ocular hypertension or open-angle glaucoma between one ICS and another. Two observational studies provide consistent evidence of a dose-related increase in risk for ICS-treated patients.

**Key Question 2 Consensus**

**The ICS Subcommittee agrees by consensus that for outpatients with asthma or COPD:**

- Evidence is inconclusive that the overall tolerability of ICSs differs substantially among ICSs.
- Evidence is inconclusive to quantify the risk of bone fractures, decreased BMD, osteoporosis, acute adrenal crisis, cataracts or open-angle glaucoma of one ICS compared to another.
- There is fair evidence that short-term growth rate (<1 year) is reduced with all ICSs, but significantly less with fluticasone as compared to beclomethasone or budesonide treatment.
- Evidence does not suggest a long-term adverse effect of reduction in adult height with any ICS within this class.

**Key Question 3** Are there subgroups of patients based on demographics (age, racial groups, gender), other medications (drug-drug interactions), co morbidities (drug-disease interactions), or pregnancy for which one inhaled corticosteroid is more effective or associated with fewer adverse events than another?

Although there were no studies comparing the efficacy and tolerability of ICSs between subgroups and the general population, there were several studies using subgroups as the population being studied and their results provide indirect evidence. Overall the strength of the evidence for comparing ICSs in terms of a variety of variables that define important subgroups is poor.

## Age

Indirect evidence suggests that ICSs do not differ in efficacy and tolerability in pediatric or older populations compared to the general population. However, only the makers of budesonide have provided studies for young children (age 1-4) for efficacy and safety to the FDA.

## Ethnicity, Gender, and Co-morbidities

No head-to-head trials assessing the impact of race, gender, co-morbidities or other drugs were found. Because mixed evidence supports an increased risk of osteoporotic fractures, cataracts, and glaucoma in ICS-treated patients especially at higher doses, ICSs should be used cautiously in elderly or at risk populations for these conditions. Insufficient evidence exists to indicate a difference in efficacy or adverse events between ICSs in patients with these subpopulation characteristics.

## Pregnancy

No study evaluated the risk of preterm delivery, congenital malformation, stillbirth, or reduction in birth weight/length for one ICS compared to another. Consistent evidence from two observational studies suggests that babies born to ICS-treated mothers are not at increased risk. Only the makers of budesonide have provided data to the FDA to obtain a category B pregnancy safety rating.

## Severe Persistent Asthma

One fair-rated trial[27] comparing mometasone with placebo assessed quality of life in 132 patients with severe persistent asthma and revealed a significantly more improved health-related quality of life that for those on placebo. ($P < 0.05$)

## Device and Dosing Regimens

Available ICSs differ in the number of puffs required to deliver an equivalent dose. A review of the available evidence was conflictive regarding the effect of device or dosing regimen on ICS adherence, persistence, effectiveness, tolerability, and patient preferences.

[27] Fish JE, Karpel JP, Craig TJ et al. Inhaled mometasone furoate reduces oral prednisone requirements whil improving respiratory function and health-related quality of life in –atients with severe persistent asthma. J Allergy Clin Immunol 2000;106(5):852-60.

**Key Question 3 Consensus**

**The ICS Subcommittee agrees by consensus that for subgroups of patients based on demographics (age, racial groups, gender), other medications (drug-drug interactions), co-morbidities (drug-disease interactions), pregnancy, or dosing requirements and device variability:**

- The overall evidence of tolerability of ICS does not differ substantially.
- The evidence is insufficient to indicate a difference between ICSs based on subpopulation characteristics.
- ICS treatment decisions should balance patient preferences for a particular device with the dosing regimen required to maintain clinical efficacy.

## *Conclusion*

**It is the decision of the ICS Subcommittee:**

1. For patients with asthma or COPD there is insufficient evidence to evaluate differences among ICSs for comparative effectiveness.
2. Conclusions about efficacy and effectiveness are difficult to extrapolate to an entire asthma population because the available evidence fails to consider the number of inhalations required to deliver equivalent doses and/or the patient's ability to comply with treatment, and the limited duration of the trials.
3. There is consistent evidence that ICSs do not reduce mortality or improve quality of life in COPD.
4. There is fair evidence that short-term growth rate (<1 year) is reduced with all ICSs, but significantly less with fluticasone as compared to beclomethasone or budesonide treatment for asthma. However, evidence does not suggest a long-term effect on reduction of adult height with any ICSs within this class.

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# Health Resources Commission

The State of Oregon's Health Resources Commission is a volunteer commission appointed by the Governor. The Health Resources Commission provides a public forum for discussion and development of consensus regarding significant emerging issues related to medical technology. Created by statute in 1991, it consists of four physicians experienced in health research and the evaluation of medical technologies and clinical outcomes; one representative of hospitals; one insurance industry representative; one business representative; one representative of labor organizations; one consumer representative; two pharmacists. All Health Resources Commissioners are selected with conflict of interest guidelines in mind. Any minor conflict of interest is disclosed.

The Commission is charged with conducting medical assessment of selected technologies, including prescription drugs. The commission may use advisory committees or subcommittees, the members to be appointed by the chairperson of the commission subject to approval by a majority of the commission. The appointees have the appropriate expertise to develop a medical technology assessment. Subcommittee meetings and deliberations are public, where public testimony is encouraged. Subcommittee recommendations are presented to the Health Resources Commission in a public forum. The Commission gives strong consideration to the recommendations of the advisory subcommittee meetings and public testimony in developing its final reports.