Drug Class Review

Quick-relief Medications for Asthma

Preliminary Scan Report #5

January 2016

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OBJECTIVE

The purpose of this preliminary updated literature scan process is to provide the Participating Organizations with a preview of the volume and nature of new research that has emerged subsequent to the previous full review process. Provision of the new research presented in this report is meant to assist with Participating Organizations' consideration of allocating resources toward a full report update, a single drug addendum, or a summary review. Comprehensive review, quality assessment, and synthesis of evidence from the full publications of the new research presented in this report would follow only under the condition that the Participating Organizations ruled in favor of a full update. The literature search for this report focuses on new randomized controlled trials and comparative effectiveness reviews as well as actions taken by the U.S. Food and Drug Administration (FDA) since the last report. Other important studies could exist.

Date of Last Update Report

Update #1, October 2008 (searches through May 2008)

Date of Last Preliminary Update Scan Report

January 2015

Scope and Key Questions

The Pacific Northwest Evidence-based Practice Center wrote preliminary key questions, identifying the populations, interventions, and outcomes of interest, and based on these, the eligibility criteria for studies. These key questions were reviewed and revised by representatives of organizations participating in the Drug Effectiveness Review Project (DERP). The participating organizations of DERP are responsible for ensuring that the scope of the review reflects the populations, drugs, and outcome measures of interest to both clinicians and patients. The participating organizations approved the following key questions to guide this review:

1. What is the comparative efficacy and effectiveness of quick-relief medications used to treat outpatients with bronchospasm due to asthma, or to prevent or treat exercise-induced bronchospasm?
2. What is the comparative incidence and severity of adverse events reported from using quick-relief medications to treat outpatients with bronchospasm due to asthma, or to prevent or treat exercise-induced bronchospasm?
3. Are there subgroups of patients for which quick-relief medications used to treat outpatients with bronchospasm due to asthma or to prevent or treat exercise-induced bronchospasm, differ in efficacy, effectiveness, or frequency and severity of adverse events?

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Inclusion Criteria

Populations

1. Adults or children with asthma including those with exercise-induced bronchospasm

Excluded populations:

1. COPD
2. Acute bronchitis
3. Bronchiectasis
4. Children < 2 years with recurrent or persistent wheezing
5. Cystic fibrosis
6. High-altitude pulmonary edema

Interventions

1. Inhaled short-acting beta$_2$-agonists (SABA)
    a. Albuterol (salbutamol in Canada) MDI and nebulizer solution
    b. Levalbuterol (R-albuterol) MDI and nebulizer solution (levalbuterol is not available in Canada)
    c. Pirbuterol (not available in Canada)
    d. Terbutaline: available only in Canada
    e. Fenoterol: available only in Canada
2. Short-acting anticholinergics
    a. Ipratropium bromide MDI and nebulizer solution
3. Combination products
    a. Ipratropium bromide with albuterol MDI or ipratropium bromide with albuterol nebulizer solution

Excluded interventions:

1. Systemic corticosteroids
    a. Prednisone
    b. Methylprednisolone
    c. Prednisolone
2. Inhaled Corticosteroids
3. Inhaled Cromolyn
4. Salmeterol
5. Long-acting anticholinergics: tiotropium
6. Studies where bronchospasm was induced by methacholine, histamine, cold
7. Combination products which include a quick-relief agent and another agent not included in this review
8. Formoterol

Effectiveness Outcomes

1. Symptoms: e.g., cough, wheezing, shortness of breath
2. Change in treatment regimen for the exacerbation
3. Healthcare utilization: length of stay in the ER or other clinical facility, need for re-treatment within 24 hours, hospital admissions, length of hospital stay

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4. For exercise induced bronchospasm: exercise tolerance, symptoms
5. Mortality

Harms Outcomes

1. Overall adverse events reported
2. Withdrawals due to adverse events
3. Serious adverse events

Setting

1. Outpatient settings including urgent care facilities and the emergency room

Study Designs (from Update Report)

1. For effectiveness: Head-to-head RCTs or controlled clinical trials with total sample size ≥ 20. No minimum duration of follow-up.
2. For adverse events: Head-to-head RCTs, controlled clinical trials, or observational studies with sample size ≥ 10. No minimum duration of follow-up.

METHODS FOR SCAN

Literature Search

To identify relevant citations, we searched Ovid MEDLINE® and Ovid MEDLINE® In-Process & Other Non-Indexed Citations from November 2014 through December 2015 using terms for specific included drugs and limits for English language and humans. Literature searches included any new drugs identified in the present scan in addition to those included in Table 1. We also searched the FDA website (http://www.fda.gov/medwatch/safety.htm) for identification of new drugs, new populations, and new serious harms (e.g., boxed warnings). To identify new drugs, we also searched CenterWatch (http://www.centerwatch.com), a privately-owned database of clinical trials information, and conducted a limited internet search. To identify comparative effectiveness reviews, we searched the websites of the Agency for Healthcare Research and Quality (http://www.ahrq.gov/) (http://www.effectivehealthcare.ahrq.gov/), the Canadian Agency for Drugs and Technology in Health (http://www.cadth.ca/), the VA Evidence-based Synthesis Program (http://www.hsrd.research.va.gov/publications/esp/reports.cfm), and University of York Centre for Reviews and Dissemination (http://www.york.ac.uk/inst/crd/crdreports.htm - "Our Publications" and "Our Databases"). All citations were imported into an electronic database (EndNote X7) and duplicate citations were removed.

Study Selection

We included only potentially relevant randomized controlled trials and comparative effectiveness reviews. One reviewer assessed abstracts of citations identified from literature searches for inclusion, using the criteria described above. Abstracts of selected comparative effectiveness reviews and head-to-head trials are in an Appendix document that is available upon request.

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RESULTS

New Drugs

Identified in this Preliminary Update Scan
Albuterol sulfate (PROAIR RESPICLICK): a beta$_2$-adremergic agonist approved March 31, 2015 and indicated for the treatment or prevention of bronchospasm in patients 12 years of age and older with reversible obstructive airway disease and prevention of exercise-induced bronchospasm in patients 12 years of age and older.

Identified in previous Preliminary Update Scans
None.

New Serious Harms (e.g. boxed warnings)

Identified in this Preliminary Update Scan
None.

Identified in previous Preliminary Update Scans
None.

Comparative Effectiveness Reviews

Identified in this Preliminary Update Scan
None.

Identified in previous Preliminary Update Scans
None.

Randomized Controlled Trials

Medline searches for the current scan resulted in 64 publications, none of which were relevant to the key questions, interventions, and populations of interest in this scan. Relevant head-to-head trials that have been identified since the last update report are included in Table 1 below. Since the last update report, we have identified a total of 8 head-to-head trials, 1 active-controlled trial, and 1 placebo-controlled trial. Five of the aforementioned head-to-head trials compared different delivery methods of the same drug (e.g., with or without a spacer, nebs vs. MDI, delivery by mask vs. by hood). Abstracts of the aforementioned head-to-head trials are available in the appendix document, which is available upon request. The abstracts of the active-controlled trial and the placebo-controlled trial are also available upon request.

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Table 1. Potentially relevant trials of drugs for quick relief of asthma symptoms (N=8)

Author, Year	Comparison	N	Focus
Head-to-head drug			
Andrews, 2009	Levalbuterol nebs Racemic albuterol nebs	81	Children aged 6-18
Punj, 2009	Levosalbutamol Racemic Salbutamol	60	Children aged 5-18
Wilkinson, 2011	Racemic albuterol nebs Levalbuterol nebs	99	Children aged 6-17
Head-to-head delivery method			
Bar-Yishay, 2011	Salbutamol 0.30 mg/kg by mask Salbutamol 0.30 mg/kg by hood	26	Wheezy infants
Direkwatanachai, 2011	Salbutamol pMDI 6 puffs with Volumatic spacer Salbutamol 6 puffs with Easyhaler (DPI) Salbutamol 0.15 mg/kg nebs	216	Children aged 5-18 in Thailand
Dhuper, 2011	Albuterol with MDI/spacer Albuterol nebs	60	Inner city adults; crossover study
Rotta, 2010	Salbutamol pMDI with spacer Salbutamol nebs	46	Children aged 1-5
Sabato, 2011	1 hour of continuous nebulized albuterol 1-time albuterol treatment with AeroEclipse breath-actuated nebulizer	149	Children aged 0-18

Active-controlled trials (N=1)
Salbutamol nebs vs. Procaterol nebs

- Mangunnegoro, 2011 (Indonesians with moderate acute asthma age 15-60)

Placebo-controlled trials (N=1)
Albuterol inhaler

- Wechsler, 2011 (crossover study)

SUMMARY

Since the last update report, we have identified one newly approved drug: albuterol sulfate (PROAIR RESPICLICK). We have identified 8 head-to-head trials (5 of which compare different delivery methods of the same drug), 1 active-controlled trial, and 1 placebo-controlled trial, none of which were identified in the present scan. We have not identified any new serious harms or comparative effectiveness reviews in current or previous scans conducted since the last update report.

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