

Inhaled Beta₂- Agonists

Key Questions and Inclusion Criteria

Key Questions

Efficacy and effectiveness

1. When used in adults with asthma or chronic obstructive pulmonary disease (COPD), are there differences in efficacy or effectiveness among long-acting, inhaled beta₂-agonists, when used in the outpatient setting?
2. When used in adults with asthma or COPD, are there differences in efficacy or effectiveness among the following short-acting inhaled beta₂-agonists when used in the outpatient setting: albuterol, levalbuterol, pirbuterol, and metaproterenol?
3. When used in children with asthma, are there differences in efficacy or effectiveness among long-acting, inhaled beta₂-agonists, when used in the outpatient setting?
4. When used in children with asthma, are there differences in efficacy or effectiveness among the following short-acting inhaled beta₂-agonists when used in the outpatient setting: albuterol, levalbuterol, pirbuterol, and metaproterenol?

Safety

5. When used in adults with asthma or COPD, are there differences in safety or rates of adverse events among long-acting, inhaled beta₂-agonists, when used in the outpatient setting?
6. When used in adults with asthma or COPD, are there differences in safety or rates of adverse events among the following short-acting inhaled beta₂-agonists when used in the outpatient setting: albuterol, levalbuterol, pirbuterol, and metaproterenol?
7. When used in children with asthma, are there differences in safety or rates of adverse events among long-acting, inhaled beta₂-agonists, when used in the outpatient setting?
8. When used in children with asthma, are there differences in safety or rates of adverse events among the following short-acting inhaled beta₂-agonists, when used in the outpatient setting: albuterol, levalbuterol, pirbuterol, and metaproterenol?

Subpopulations

9. Are there subgroups of patients based on demographic characteristics (age, racial groups, gender), other medications (drug-drug interactions), comorbidities (drug-disease interactions), or pregnancy for which one long-acting, inhaled beta₂-agonist is more efficacious, effective, or associated with fewer adverse events than another inhaled beta₂-agonist?
10. Are there subgroups of patients based on demographic characteristics (age, racial groups, gender), other medications (drug-drug interactions), comorbidities (drug-disease interactions), or pregnancy for which one of the following short-acting, inhaled beta₂-agonists is more efficacious, effective, or associated with fewer adverse events: albuterol, levalbuterol, pirbuterol, and metaproterenol?

Inclusion Criteria

Populations

- Adult or pediatric outpatients with asthma
 - Chronic (maintenance) therapy
 - Acute (rescue) therapy
- Adult outpatients with COPD

Interventions

Long-acting

- Salmeterol xinafoate = Serevent Discus
- Formoterol fumarate = Foradil, Oxeze

Short-acting

- Albuterol = ventolin, ventolin HFA, proventil, albuterol HFA
- Albuterol sulfate = proventil HFA
- Levalbuterol HCL= Xopenex (not available in Canada)
- Metaproterenol = alupent
- Pirbuterol acetate= maxair autoinhaler
- Terbutaline= Bricanyl (Canada)
- Fenoterol = Berotec (Canada)

Method of delivery

- All approved methods of delivery will be considered for each of these drugs: metered-dose inhaler (aerosol), discus, solution (nebulizer), products using HFA

Effectiveness outcomes

- Symptoms (e.g., cough, wheezing, shortness of breath)
- Functional capacity; quality of life; ability to participate in work, school, or sports
- Emergency department or urgent medical care visits
- Hospitalizations
- Mortality
- Change in concurrent medication use (inhaled steroids, oral steroids, antibiotics)

Safety outcomes

- Overall adverse effects reported
- Withdrawals due to adverse effects
- Serious adverse events reported (e.g., acute bronchospasm, significant changes in blood pressure, cardiac arrhythmias, hypokalemia, etc.)
- Specific adverse events or withdrawals due to specific adverse events

Study designs

- For efficacy and effectiveness: randomized controlled trials and systematic reviews
- For safety: randomized controlled trials, controlled clinical trials, and observational studies

Comparisons

- Initially only head-to-head comparison studies will be examined, due to the anticipated extensive literature available

- If information from direct (head-to-head) comparisons is not sufficient to address the Key Questions, indirect evidence will be identified and synthesized (comparisons of placebo- and active-controlled trials involving the included beta₂-agonists)

Exclusion criteria

Populations or conditions

- Acute bronchitis
- Bronchiectasis
- Children less than 2 years with recurrent or persistent wheeze
- Cystic fibrosis
- High-altitude pulmonary edema