

## **Controller Medications for Asthma**

### Key Questions and Inclusion Criteria

#### **Key Questions**

1. What is the comparative efficacy and effectiveness of controller medications used to treat outpatients with persistent asthma?
2. What is the comparative tolerability and frequency of adverse events for controller medications used to treat outpatients with persistent asthma?
3. Are there subgroups of these patients based on demographics (age, racial groups, gender), asthma severity, comorbidities (drug-disease interactions, including obesity), other medications (drug-drug interactions), smoking status, genetics, or pregnancy for which asthma controller medications differ in efficacy, effectiveness, or frequency of adverse events?

#### **Inclusion Criteria**

##### Populations

- Adult or pediatric outpatients with persistent asthma

##### Interventions

1. Inhaled corticosteroids:
  - a. Beclomethasone (Qvar, Vanceril)
  - b. Budesonide [Pulmicort Turbuhaler (powder), Pulmicort Flexhaler, Pulmicort Respules (suspension), Pulmicort Nebuamp]
  - c. Flunisolide (AeroBid, AeroBid-M, AeroSpan, Bronalide)
  - d. Fluticasone [Flovent (aerosol), Flovent Rotadisk (powder), Flovent Diskus (powder), Flovent HFA]
  - e. Triamcinolone (Azmacort)
  - f. Mometasone (Asmanex Twisthaler)
2. Long-acting beta-2 agonists (LABAs)
  - a. Formoterol (Foradil Certihaler, Foradil Aerolizer, Foradil (dry powder capsule), Oxis, Perforomist (solution), Oxeze Turbuhaler)
  - b. Arformoterol ((R, R)-formoterol stereoisomer, Brovana)
  - c. Salmeterol (Serevent, Serevent Diskhaler, Serevent Diskus)
3. Leukotriene modifiers (leukotriene receptor antagonists (LTRAs) and leukotriene synthesis inhibitors (LTSIs))
  - a. Montelukast (Singulair)
  - b. Zafirlukast (Accolate)
  - c. Zileuton (Zyflo, Zyflo CR)
4. Anti-IgE therapy
  - a. Omalizumab (Xolair)
5. Combination products
  - a. Fluticasone propionate/Salmeterol xinafoate (Advair, Advair Diskus, Advair HFA)
  - b. Budesonide/formoterol (Symbicort, Symbicort Turbuhaler)

Efficacy and Effectiveness outcomes

- Control of symptoms (e.g., days/nights/frequency of symptoms, rate of asthma exacerbations, frequency of rescue medication use, courses of oral steroids)
- Functional capacity and quality of life (missed school and missed work days, ability to participate in work/school/sports/physical activity, activity limitation, improved sleep/sleep disruption)
- Urgent care services (Emergency department visits/urgent medical care visits)
- Adherence
- Hospitalization
- Mortality

Adverse Events/Safety outcomes

- Overall adverse events reported
- Withdrawals due to adverse events
- Serious adverse events reported (e.g., growth suppression, hypothalamus-pituitary-adrenal axis suppression, osteoporosis/fractures, mortality)
- Specific adverse events or withdrawals due to specific adverse events (e.g. growth retardation, bone mineral density, ocular toxicity, suppression of the HPA axis, tachycardia, anaphylaxis, death)

Study designs

- For efficacy and effectiveness, randomized controlled trials of at least 6 weeks duration ( $n \geq 40$ ) and good-quality systematic reviews
- For adverse events/safety, randomized controlled trials of at least 6 weeks ( $n \geq 40$ ) and observational studies of at least 6 months duration ( $n \geq 100$ )