Tiotropium has been studied in adults with uncontrolled asthma and compared to salmeterol, doubling the dose of ICS, and as add-on to LABA-ICS combination. The studies have been short-term and no effect on exacerbations have been reported:

- Peters et al NEJM 2010;
- One study showed comparable BD effects w/no changes in asthma control
  - Kerstjens JACI 2011
- One study showed that adding tiotropium to patients who were not controlled on LABA-ICS combos improved lung function but not symptoms
  - Bateman JACI 2011
WARNING: ASTHMA-RELATED DEATH

See full prescribing information for complete boxed warning.

• Long-acting beta₂-adrenergic agonists (LABAs), such as salmeterol, one of the active ingredients in ADVAIR DISKUS, increase the risk of asthma-related death. A US study showed an increase in asthma-related deaths in patients receiving salmeterol (13 deaths out of 13,176 patients treated for 28 weeks on salmeterol versus 3 out of 13,179 patients on placebo). Currently available data are inadequate to determine whether concurrent use of inhaled corticosteroids or other long-term asthma control drugs mitigates the increased risk of asthma-related death from LABAs. Available data from controlled clinical trials suggest that LABAs increase the risk of asthma-related hospitalization in pediatric and adolescent patients. (5.1)

• When treating patients with asthma, only prescribe ADVAIR DISKUS for patients not adequately controlled on a long-term asthma control medication, such as an inhaled corticosteroid, or whose disease severity clearly warrants initiation of treatment with both an inhaled corticosteroid and a LABA. Once asthma control is achieved and maintained, assess the patient at regular intervals and step down therapy (e.g., discontinue ADVAIR DISKUS) if possible without loss of asthma control and maintain the patient on a long-term asthma control medication, such as an inhaled corticosteroid. Do not use ADVAIR DISKUS for patients whose asthma is adequately controlled on low- or medium-dose inhaled corticosteroids. (1.1, 5.1)
# SMART Study

## Table 1. SMART Results

<table>
<thead>
<tr>
<th>SMART Patients</th>
<th>Asthma-Related Deaths in Salmeterol Group n (%)</th>
<th>Asthma-Related Deaths in Placebo Group n (%)</th>
<th>Relative Risk of Asthma-Related Death (95% Confidence Interval)</th>
<th>Excess Deaths Expressed per 10,000 Patients+ (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Patients§</td>
<td>13 (0.10%)</td>
<td>3 (0.02%)</td>
<td>4.37 (1.25, 15.34)</td>
<td>8 (3, 13)</td>
</tr>
</tbody>
</table>
| salmeterol: n = 13,176  
placebo: n = 13,179 |                                              |                                             |                                                               |                                                                     |
| Caucasian Patients | 6 (0.07%)                                    | 1 (0.01%)                                   | 5.82 (0.70, 48.37)                                           | 6 (1, 10)                                                           |
| Salmeterol: n = 9,281  
Placebo: n = 9,361 |                                              |                                             |                                                               |                                                                     |
| African American Patients | 7 (0.31%)                                    | 1 (0.04%)                                   | 7.26 (0.89, 58.94)                                           | 27 (8, 46)                                                          |
| Salmeterol: n = 2,366  
Placebo: n = 2,319 |                                              |                                             |                                                               |                                                                     |
ICS and the GINA Guidelines December 2011

Figure 4.3.2.
Management Approach Based On Control
For Children Older Than 5 Years, Adolescents and Adults

<table>
<thead>
<tr>
<th>Level of Control</th>
<th>Treatment Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controlled</td>
<td>Maintain and find lowest controlling step</td>
</tr>
<tr>
<td>Partly controlled</td>
<td>Consider stepping up to gain control</td>
</tr>
<tr>
<td>Uncontrolled</td>
<td>Step up until controlled</td>
</tr>
<tr>
<td>Exacerbation</td>
<td>Treat as exacerbation</td>
</tr>
</tbody>
</table>

Asthma education. Environmental control.
(If step-up treatment is being considered for poor symptom control, first check inhaler technique, check adherence, and confirm symptoms are due to asthma.)

<table>
<thead>
<tr>
<th>Treatment Steps</th>
</tr>
</thead>
<tbody>
<tr>
<td>Step 1</td>
</tr>
<tr>
<td>Step 2</td>
</tr>
<tr>
<td>Step 3</td>
</tr>
<tr>
<td>Step 4</td>
</tr>
<tr>
<td>Step 5</td>
</tr>
</tbody>
</table>

As needed rapid-acting β₂-agonist

<table>
<thead>
<tr>
<th>Controller options***</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-dose Inhaled ICS*</td>
</tr>
<tr>
<td>Leukotriene modifier**</td>
</tr>
<tr>
<td>Low-dose ICS plus sustained release theophylline</td>
</tr>
</tbody>
</table>

As needed rapid-acting β₂-agonist

<table>
<thead>
<tr>
<th>Controller options***</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-dose ICS plus long-acting β₂-agonist</td>
</tr>
<tr>
<td>Medium-or high-dose ICS plus long-acting β₂-agonist</td>
</tr>
<tr>
<td>Medium-or high-dose ICS</td>
</tr>
<tr>
<td>Low-dose ICS plus leukotriene modifier</td>
</tr>
<tr>
<td>Leukotriene modifier</td>
</tr>
<tr>
<td>Sustained release theophylline</td>
</tr>
<tr>
<td>Anti-IgE treatment</td>
</tr>
</tbody>
</table>

* ICS = inhaled glucocorticosteroids
** = Receptor antagonist or synthesis inhibitors
*** = Recommended treatment (shaded boxes) based on group mean data. Individual patient needs, preferences, and circumstances (including costs) should be considered.

Alternative reliever treatments include inhaled anticholinergics, short-acting oral β₂-agonists, some long-acting β₂-agonists, and short-acting theophylline.

Regular dosing with short and long-acting β₂-agonists is not advised unless accompanied by regular use of an inhaled glucocorticosteroid.
**Generic montelukast August 2012**


- Apotex, Aurobindo, Endo, Kudco, Mylan, Roxane, Sandoz, Teva, and Torrent have received approval for chewable tablets.

- Teva has received approval for the oral granule form.
Figure 2.3. Association Between Symptoms, Spirometric Classification, and Future Risk of Exacerbations

When assessing risk, choose the highest risk according to GOLD grade or exacerbation history.

<table>
<thead>
<tr>
<th>Risk</th>
<th>GOLD Classification of Airflow Limitation</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>(C)</td>
</tr>
<tr>
<td>3</td>
<td>(A)</td>
</tr>
<tr>
<td>2</td>
<td>(D)</td>
</tr>
<tr>
<td>1</td>
<td>(B)</td>
</tr>
</tbody>
</table>

Symptoms
(mMRC or CAT score)

- mMRC 0-1
- CAT < 10
- mMRC > 2
- CAT ≥ 10

Risk
- ≥ 2
- 1
- 0

Exacerbation history
RECENTLY APPROVED HFA INCS

- Beclomethasone HFA (QNASL®)
  - ≥12 yo, SAR/PAR, 2sp/n/d (80mcg/sp), Preg C
  - AE: nasal discomfort, erosion 4/415, epistaxis 1.9-11%

- Ciclesonide HFA (Zetonna®)
  - ≥12 yo, SAR/PAR, 1sp/n/d (37mcg/sp), Preg C
  - □ TOSS (instantaneous and reflective) in SAR study
  - AE:nasal discomfort (5.7%; epistaxis up to 11.4% nasal septal ulceration

NEW HFA INCS: PATIENT SELECTION

- Prefer dry
- Failed with aqueous
- Poor tolerance AQ: run down/out, sore throat
- Rhinorrhea
- Poor activation/inhalation coordination
- ? Sinusitis
  - Smaller molecule, better penetration to ostia

Luskin AT Allergy Asthma Proc 2011;32:168-77;
Hankin CS Allergy Asthma Proc 2012;33:258-64
INCS/Antihistamine Nasal Spray

- Fluticasone dipropionate/azelastine (Dymista®)
  - SAR individuals requiring both azelastine and INCS
  - ≥12 yo, 1 sp(137mcg/50mcg) q nostril bid
  - Onset within 30 min
  - AE characteristic of each component: dysgeusia 4%, epistaxis 2% (=Pbo), headache, nasal congestion, rhinitis, pharyngitis

Dymista PI; Carr W JACI 2012;129:1282-9
TREATMENT OF ACUTE SINUSITIS: IDSA GUIDELINES 2012

- When to treat: severe; persistent; ‘double sickening’
- Higher risk: severe symptoms; daycare, age<2>65yr, recent hospitalization, ABX past month, risk of complications, immunocompromised
- First line: Amox/Clav (in high dose those non-susceptible to low dose)
  - (alt. doxycycline—Preg D)
  - PCN allergy use FQ or clinda = 3rd gen ceph if non-Ige mediated allergy)
  - Duration 5-7d adult; 10-14d children
  - Consider Dx or Tx failure after 48-72hr on Tx
  - Not recommended as empiric therapy: Amox; TMP/sulfa, macrolide; 2nd-3rd gen ceph

Chow AW. Clin Inf Dis (3/12) e1-e41 accessed at http://cid.oxfordjournals.org
ADJUNCTS IN ABRS

- Nasal saline rinse
  - isotonic=hypertonic in efficacy, but isotonic less AE
  - do not use well water or plain tap water
  - Add baby shampoo or budesonide*?

- INS: helpful if co-morbid AR

- Not recommended: topical or oral decongestants, anti-histamines

- Referral to specialist (ENT, All, ID) severe, persistent, recurrent, chronic RS

AOM: Treat or Not to Treat

- Clear diagnosis is critical (otoscopy, symptoms)
- Treat pain (ibu, tyl, anesthetic [>2yr]—lack data for home remedies (distraction, heat or cold, oil in EAC); No decongestants, antihistamines
- Treat with appropriate ABX/dosing x 5-7d (>6yo) - 10d (<5yo)
- Cochrane (and most of Europe): observation x 72 hr
  - Except: <2yo, bilat AOM, otorrhea
  - AEs: diarrhea, rash, develop bacterial resistance
- Hoberman: small but significant differences Tx (amox/clav 90mg/kg) vs Pbo
  - Time to improvement, resolution, clinical cure, relapse
- UpToDate:
  - Mild/uncertain disease: observe
  - Treat <6mo old; suggest in 6-24mo; >24mo with bilat disease or otorrhea