Quick Reference from the Working Group Report on Managing Asthma During Pregnancy: Recommendations for Pharmacologic Treatment

Update 2004*

Managing Asthma During Pregnancy: Recommendations for Pharmacologic Treatment

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Maintaining adequate control of asthma during pregnancy is important for the health and well-being of both the mother and her baby. Asthma has been reported to affect 3.7 to 8.4 percent of pregnant women, making it potentially the most common serious medical problem to complicate pregnancy. The largest and most recent studies suggest that maternal asthma increases the risk of perinatal mortality, preclampsia, preterm birth, and low birth weight infants. More severe asthma is associated with increased risks, while better-controlled asthma is associated with decreased risks.

In 1993, the National Asthma Education and Prevention Program (NAEPP) published the Report of the Working Group on Asthma and Pregnancy (Asthma and Pregnancy Report 1993), which presented recommendations for the management of asthma during pregnancy. Since then, there have been revisions to the general asthma treatment guidelines, Guidelines for the Diagnosis and Management of Asthma—Update 2000,23 and Expert Panel Report 2 (EPR-2) 1997 and EPR—Update 2002 relative to other aspects of asthma care are also presented because they should enhance the overall success and safety of managing asthma in pregnancy.

Systematic Review of the Evidence

A systematic review of the evidence on the safety of asthma medications during pregnancy was conducted by drug class. Of 226 articles retrieved in the search of literature published in peer-reviewed journals from January 1990 through May 2003, 42 met criteria for inclusion in the evidence review; 2 additional articles published after May 2003 were included, for a total of 44 articles. A summary of the findings from the evidence, arranged by medication category, follows.

Beta₂-Agonists

One experimental animal study6 and six human studies were included. The six human studies consisted of one case report10 and five clinical studies11–15 that included a total of 6,667 pregnant women, of whom 1,929 had asthma and 1,599 had taken beta₂-agonists. The data were reassuring regarding the safety of beta₂-agonists during pregnancy. More data were available for albuterol. Two long-acting inhaled beta₂-agonists have become available since 1993—salmeterol and formoterol. Limited data are available on their use during pregnancy. The pharmacologic and toxicologic profiles of these two drugs are similar to the short-acting inhaled beta₂-agonists, with the exception of their prolonged retention in the lungs.

Theophylline

Seven experimental animal studies16–22 and eight human studies were included. The experimental animal studies confirm the association of high-dose theophylline and adverse pregnancy outcomes in animals. The eight human studies, consisting of two case reports23, 24 and six clinical studies11, 13, 25–28 (of which two were randomized controlled trials), included a total of 57,163 pregnant women, of whom 3,616 had asthma and 660 had taken theophylline. Studies and clinical experience confirm the safety of theophylline at recommended doses (to serum concentration of 5–12 mcg/mL) during pregnancy. In a randomized controlled trial, there were no differences in asthma exacerbations or maternal or perinatal outcomes in the theophylline versus the beclomethasone dipropionate treatment groups.

However, in the theophylline treatment group, there were higher levels of reported side effects and discontinuation of the medication and an increase in the proportion of women with forced expiratory volume in 1 second (FEV₁) at less than 80 percent of that predicted.

Anticholinergics

No data on anticholinergics were available for the current evidence review.

Inhaled corticosteroids

Three experimental animal studies29–31 and 10 human studies were included. The human studies included eight studies of pregnant women. Of the eight studies, five were cohort studies11, 13, 22–24 one was a controlled trial;28 and two were randomized controlled trials.25, 28 These eight studies included a total of 21,072 pregnant women, of whom 16,900 had asthma and 6,113 had taken inhaled corticosteroids. Also included were two studies of newborns from the Swedish Birth Registry—one compared the rate of abnormalities among 2,014 newborns whose mothers had taken budesonide to the rate of abnormalities in the total newborn population, although the number in that population was not reported;36 the other study compared 2,900 newborns whose mothers had taken budesonide to the total newborn population of 293,948;37 there may be some overlap in the populations of these two studies. There are three major conclusions from the evidence review: (1) the risk of asthma exacerbations associated with pregnancy can be reduced and lung function (FEV₁) improved with the use of inhaled corticosteroid therapy;25, 28, 34 (2) no studies...
to date, including studies of large birth registries, have related inhaled corticosteroid use to any increases in congenital malformations or other adverse perinatal outcomes; and (3) the preponderance of data on inhaled corticosteroids during pregnancy is with budesonide. Few or no studies are available on the other inhaled corticosteroid formulations during pregnancy.

**Oral (systemic) corticosteroids**

Nine experimental animal studies and eight human studies were included. The animal studies do not change the previous understanding (Asthma and Pregnancy Report 1993) of the steroid-mediated clefting or decreases in fetal growth in animals. The eight human studies in the current evidence review included one report of two meta-analyses: one meta-analysis used six cohort studies that included 51,380 pregnant women, of whom 535 had taken oral corticosteroids; the other meta-analysis used four case-control studies, each of which was also eligible to be included in the evidence review. These four case-control studies included 52,038 pregnant women, of whom 25 had taken oral corticosteroids. The remaining three human studies included one case-control study and two prospective cohort studies, that included a total of 4,321 pregnant women, of whom 1,998 had asthma and 213 had taken oral corticosteroids. The findings from the current evidence review are conflicting. Oral corticosteroid use, especially during the first trimester of pregnancy, is associated with an increased risk for isolated cleft lip with or without cleft palate (the risk in the general population is 0.1 percent; the risk in women on oral corticosteroids is 0.3 percent). However, very few pregnant women who had oral steroid-dependent asthma were included in the studies, and the length, timing, and dose of exposure to the drug were not well described. Oral corticosteroid use during pregnancy in patients who have asthma is associated with an increased incidence of preeclampsia and the delivery of both preterm and low birth weight infants. However, the available data make it difficult to separate the effects of the oral corticosteroids on these outcomes from the effects of severe or uncontrolled asthma, which has been associated with maternal and/or fetal mortality.

**Cromolyn**

No experimental animal studies and two human studies were included in the current review. The two human studies consisted of prospective cohort studies that included 4,110 pregnant women, of whom 1,917 had asthma and 318 had taken cromolyn. The safety of using cromolyn during pregnancy is supported by the current review of evidence.

**Leukotriene modifiers**

Leukotriene modifiers include two compounds available as oral tablets (the receptor antagonists montelukast and zafirlukast) and 5-lipoxygenase pathway inhibitors (e.g., zileuton). No animal studies and one human study were available for review. The human study was an observational study of 2,205 pregnant women, 873 with asthma, of whom 9 took leukotriene modifiers, but the specific agent was not identified. The conclusion is that minimal data are currently available on the use of leukotriene modifiers during pregnancy. Reassuring animal studies have been submitted to the Food and Drug Administration (FDA) for leukotriene receptor antagonists but not for the leukotriene lipoxigenase inhibitor.

**Recommendations for Managing Asthma During Pregnancy**

The Working Group recommends the following principles and stepwise approach to pharmacologic therapy for managing asthma during pregnancy. (See figures 1–6.) The principles and approach are based on the Working Group’s interpretation of the current scientific review of the evidence on the safety of asthma medications during pregnancy and consideration of previous NAEPP reports: the Asthma and Pregnancy Report 1993, the EPR-2 1997, and the EPR—Update 2002.

**General principles**

- The treatment goal for the pregnant asthma patient is to provide optimal therapy to maintain control of asthma for maternal health and quality of life as well as for normal fetal maturation. Asthma control is defined as:
  - M inimal or no chronic symptoms day or night
  - M inimal or no exacerbations
  - N o limitations on activities
  - M aintenance of (near) normal pulmonary function
  - M inimal use of short-acting inhaled beta,-agonist
  - M inimal or no adverse effects from medications

- It is safer for pregnant women with asthma to be treated with asthma medications than for them to have asthma symptoms and exacerbations. M onitoring and making appropriate adjustments in therapy may be required to maintain lung function and, hence, blood oxygenation that ensures oxygen supply to the fetus. Inadequate control of asthma is a greater risk to the fetus than asthma medications are. Proper control of asthma should enable a woman with asthma to maintain a normal pregnancy with little or no risk to her or her fetus.

- The obstetrical care provider should be involved in asthma care, including monitoring of asthma status during prenatal visits. A team approach is helpful if more than one clinician is managing a pregnant woman with asthma.

- Asthma treatment is organized around four components of management:
  - A ssessment and monitoring of asthma, including objective measures of pulmonary function. Because the course of asthma changes for about two-thirds of women during pregnancy, monthly evaluations of asthma history and pulmonary function are recommended. Spirometry tests are recommended at the time of initial assessment. For routine monitoring at most subsequent followup outpatient visits, spirometry is preferable, but measurement of peak expiratory flow (PEF) with a peak flow meter is generally sufficient. Patients should be instructed to be attentive to fetal activity. Serial ultrasound examinations starting at 32 weeks gestation may be considered for patients who have suboptimally controlled asthma and for women with moderate-to-severe asthma. Ultrasound examinations are also helpful after recovery from a severe exacerbation.
- Control of factors contributing to asthma severity. Identifying and controlling or avoiding such factors as allergens and irritants, particularly tobacco smoke, that contribute to asthma severity can lead to improved maternal well-being with less need for medications. (See figure 7.)

- Patient education. Asthma control is enhanced by ensuring access to education about asthma and about the skills necessary to manage it—such as self-monitoring, correct use of inhalers, and following a plan for managing asthma long term and for promptly handling signs of worsening asthma.

- A stepwise approach to pharmacologic therapy. In this approach to achieving and maintaining asthma control, the dose and number of medications and the frequency of administration are increased as necessary, based on the severity of the patient’s asthma, and are decreased when possible.

Recommendations for Pharmacologic Treatment of Asthma During Pregnancy

Stepwise approach for managing asthma. To develop recommendations for the stepwise approach to the pharmacologic treatment of asthma in pregnant women, the Working Group first considered the stepwise approach in the EPR—Update 2002, which was based on systematic review of the evidence from medication effectiveness studies in nonpregnant adults and children. The Working Group also considered EPR-2 1997 and the Asthma and Pregnancy Report 1993.

The effectiveness of medications is assumed to be the same in pregnant women as in nonpregnant women, although there are no studies that directly test this assumption. Based on their current systematic review of evidence from safety studies of asthma medications during pregnancy, the Working Group then tailored existing recommendations for stepwise therapy. Refer to figures 1, 2, and 3 for a complete list of recommended therapies and medication dosages in the stepwise approach to managing asthma. The following information highlights the rationale for the preferred medications.

- Step 1: Mild Intermittent Asthma. Short-acting bronchodilators, particularly short-acting inhaled beta2-agonists, are recommended as quick-relief medication for treating symptoms as needed in patients with intermittent asthma. Albuterol is the preferred short-acting inhaled beta2-agonist because it has an excellent safety profile and the greatest amount of data related to safety during pregnancy of any currently available inhaled beta2-agonist. Women’s experience with these drugs is extensive, and no evidence has been found either of fetal injury from the use of short-acting inhaled beta2-agonists or of contraindication during lactation.

- Step 2: Mild Persistent Asthma. The preferred treatment for long-term-control medication in Step 2 is daily low-dose inhaled corticosteroid. This preference is based on the strong effectiveness data in nonpregnant women and as well as effectiveness and safety data in pregnant women that show no increased risk of adverse perinatal outcomes. Budesonide is the preferred inhaled corticosteroid because more data are available on using budesonide in pregnant women than are available on other inhaled corticosteroids, and the data are reassuring. It is important to note that there are no data indicating that the other inhaled corticosteroid preparations are unsafe during pregnancy. Therefore, inhaled corticosteroids other than budesonide may be continued in patients who were well controlled by these agents prior to pregnancy, especially if it is thought that changing formulations may jeopardize asthma control. Cromlyn, leukotriene receptor antagonists, and theophylline are listed as alternative but not preferred therapies. Cromlyn has an excellent safety profile, but it has limited effectiveness compared with inhaled corticosteroids. Leukotriene receptor antagonists have been demonstrated to provide statistically significant but modest improvements in children and nonpregnant adults with asthma, although in studies comparing overall efficacy of the two drugs, most outcomes clearly favor inhaled corticosteroids. Published data are minimal on using leukotriene receptor antagonists during pregnancy; however, animal safety data submitted to the FDA are reassuring. Thus, leukotriene receptor antagonists are an alternative but not preferred treatment for pregnant women whose asthma was successfully controlled with this medication prior to their pregnancy. Theophylline has demonstrated clinical effectiveness in some studies and has been used for years in pregnant women with asthma. It also, however, has the potential for serious toxicity resulting from excessive dosing and/or select drug-drug interactions (e.g., with erythromycin). Using theophylline during pregnancy requires careful titration of the dose and regular monitoring to maintain the recommended serum theophylline concentration range of 5–12 mcg/mL.

- Step 3: Moderate Persistent Asthma. Two preferred treatment options are noted: either a combination of low-dose inhaled corticosteroid and a long-acting inhaled beta2-agonist, or increasing the dose of inhaled corticosteroid to the medium dose range. No data from studies during pregnancy clearly delineate that one option is recommended over the other.

Limited data describe the effectiveness and/or safety of using combination therapy during pregnancy, but strong evidence from randomized controlled trials in nonpregnant adults shows that adding long-acting inhaled beta2-agonist to a low dose of inhaled corticosteroid provides greater asthma control than only increasing the dose of corticosteroid. The pharmacologic and toxicologic profiles of long-acting and short-acting inhaled beta2-agonists are similar; there is justification for expecting long-acting inhaled beta2-agonists to have a safety profile similar to that of albuterol, for which there are data related to safety during pregnancy. Two long-acting inhaled beta2-agonists are available—salmeterol and formoterol. Limited observational data exist on their use during pregnancy; salmeterol might be chosen because it has been available longer in the United States.

Increasing the dose of inhaled corticosteroid to medium dose will benefit many patients, and, as noted previously, the data on using inhaled corticosteroids during pregnancy—including studies of large birth registries—are reassuring.

- Step 4: Severe Persistent Asthma. If additional medication is required after carefully assessing patient technique and adherence with using Step 3...
medication, then the inhaled corticosteroid dose should be increased within the high-dose range, and the use of budesonide is preferred. If this is insufficient to manage asthma symptoms, then the addition of systemic corticosteroid is warranted; although the data are uncertain about some risks of oral corticosteroids during pregnancy, severe uncontrolled asthma poses a definite risk to the mother and fetus.

Management of acute exacerbations. Asthma exacerbations have the potential to lead to severe problems for the fetus. Therefore, asthma exacerbations during pregnancy should be managed aggressively. Refer to figure 4 for home treatment of asthma exacerbation, figure 5 for emergency department and hospital management, and figure 6 for medications and dosages.

Pharmacologic management of allergic rhinitis. Rhinitis, sinusitis, and gastroesophageal reflux are conditions that are often associated with asthma, are frequently more troublesome during pregnancy, and may exacerbate coexisting asthma. If these conditions are present, appropriate treatment is an integral part of asthma management. These topics were outside the scope of the current evidence-based review, but relevant studies on the safety of rhinitis medications during pregnancy were reviewed in order to present the following recommendations.

- Intranasal corticosteroids are the most effective medications for the management of allergic rhinitis and have a low risk of systemic effect when used at recommended doses. Montelukast, a leukotriene receptor antagonist, can be used for the treatment of allergic rhinitis—but minimal data are available on the use of this medication during pregnancy.
- The current second-generation antihistamines of choice are loratadine or cetirizine.
- There may be a relationship between use of oral decongestants in early pregnancy and a rare birth defect, gastroschisis; however, the absolute risk of gastroschisis in exposed fetuses is still extremely small. If nasal decongestion is indicated in early pregnancy, an external nasal dilator, short-term topical oxymetazoline, or intranasal corticosteroid can be considered before use of oral decongestants.
### Stepwise Approach for Managing Asthma During Pregnancy and Lactation: Treatment

#### Classify Severity: Clinical Features Before Treatment or Adequate Control

<table>
<thead>
<tr>
<th></th>
<th>Symptoms/Day</th>
<th>PEF or FEV1</th>
<th>Symptoms/Night</th>
<th>PEF Variability</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Step 4</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>Continual</td>
<td>≤60%</td>
<td>Frequent</td>
<td>&gt;30%</td>
</tr>
<tr>
<td>Persistent</td>
<td></td>
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#### Medications Required To Maintain Long-Term Control

**Daily Medications**

- **Preferred treatment:**
  - High-dose inhaled corticosteroid AND
  - Long-acting inhaled beta2-agonist AND, if needed,
  - Corticosteroid tablets or syrup long term (2 mg/kg per day, generally not to exceed 60 mg per day). (Make repeat attempts to reduce systemic corticosteroid and maintain control with high-dose inhaled corticosteroid.*)

- **Alternative treatment:**
  - High-dose inhaled corticosteroid* AND
  - Sustained release theophylline to serum concentration of 5–12 mcg/mL.

- **Preferred treatment:**
  - Low-dose inhaled corticosteroid* and long-acting inhaled beta2-agonist OR
  - Medium-dose inhaled corticosteroid.*
  - Use of short-acting inhaled beta2-agonist‡ >2 times a week in intermittent asthma (daily, or increasing use in persistent asthma) may indicate the need to initiate (increase) long-term-control therapy.

- **Alternative treatment:**
  - Low-dose inhaled corticosteroid* and either theophylline or leukotriene receptor antagonist† OR sustained-release theophylline to serum concentration of 5–12 mcg/mL.

- **Preferred treatment:**
  - Low-dose inhaled corticosteroid.*

- **Alternative treatment (listed alphabetically):** cromolyn, leukotriene receptor antagonist† OR sustained-release theophylline to serum concentration of 5–12 mcg/mL.

#### Quick Relief All Patients

- Short-acting bronchodilator: 2–4 puffs short-acting inhaled beta2-agonist‡ as needed for symptoms.
- Intensity of treatment will depend on severity of exacerbation; up to 3 treatments at 20-minute intervals or a single nebulizer treatment as needed. Course of systemic corticosteroid may be needed.
- Use of short-acting inhaled beta2-agonist‡ >2 times a week in intermittent asthma (daily, or increasing use in persistent asthma) may indicate the need to initiate (increase) long-term-control therapy.

### Goals of Therapy: Asthma Control

- M inimal or no chronic symptoms day or night
- M inimal or no exacerbations
- N o limitations on activities; no school/work missed
- M aintain (near) normal pulmonary function
- M inimal use of short-acting inhaled beta2-agonist
- M inimal or no adverse effects from medications

### Notes

- The stepwise approach is meant to assist, not replace, the clinical decisionmaking required to meet individual patient needs.
- Classify severity: assign patient to most severe step in which any feature occurs (PEF is percent of personal best; FEV1 is percent predicted).
- Gain control as quickly as possible (consider a short course of systemic corticosteroid), then step down to the least medication necessary to maintain control.
- M inimize use of short-acting inhaled beta2-agonist (e.g., use of approximately one canister a month even if not using it every day indicates inadequate control of asthma and the need to initiate or intensify long-term-control therapy).
- Provide education on self-management and controlling environmental factors that make asthma worse (e.g., allergens, irritants).
- Refer to an asthma specialist if there are difficulties controlling asthma or if Step 4 care is required. Referral may be considered if Step 3 care is required.

* There are more data on using budesonide during pregnancy than on using other inhaled corticosteroids.
† There are minimal data on using leukotriene receptor antagonists in humans during pregnancy, although there are reassuring animal data submitted to FDA.
‡ There are more data on using albuterol during pregnancy than on using other short-acting inhaled beta2-agonists.
Inhaled Corticosteroids (See Estimated Comparative Daily Dosages for Inhaled Corticosteroids [Figure 3].)

### Usual Dosages for Long-Term-Control Medications During Pregnancy and Lactation*

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosage Form</th>
<th>Adult Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Systemic Corticosteroids</strong> (Applies to all three corticosteroids.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>2, 4, 8, 16, 32 mg tablets</td>
<td>• 7.5–60 mg daily in a single dose in a.m. or qod as needed for control</td>
</tr>
<tr>
<td></td>
<td>5 mg tablets, 5 mg/5 cc, 15 mg/5 cc</td>
<td>• Short-course &quot;burst&quot; to achieve control: 40-60 mg per day as single dose or 2 divided doses for 3-10 days</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>5, 10, 20, 50 mg tablets</td>
<td></td>
</tr>
<tr>
<td>Prednisone</td>
<td>5 mg/cc, 5 mg/5 cc</td>
<td></td>
</tr>
</tbody>
</table>

Long-Acting Inhaled Beta2-Agonists (Should not be used for symptom relief or for exacerbations. Use with inhaled corticosteroids.)

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosage Form</th>
<th>Adult Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salmeterol</td>
<td>MDI 21 mcg/puff</td>
<td>2 puffs q 12 hours</td>
</tr>
<tr>
<td></td>
<td>DPI 50 mcg/blister</td>
<td>1 blister q 12 hours</td>
</tr>
<tr>
<td>Formoterol</td>
<td>DPI 12 mcg/single-use capsule</td>
<td>1 capsule q 12 hours</td>
</tr>
</tbody>
</table>

Combined Medication

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosage Form</th>
<th>Adult Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluticasone/Salmeterol</td>
<td>DPI 100, 250, or 500 mcg</td>
<td>1 inhalation bid; dose depends on severity of asthma</td>
</tr>
<tr>
<td>Cromolyn</td>
<td>MDI 1 mg/puff</td>
<td>2-4 puffs tid-qid</td>
</tr>
<tr>
<td></td>
<td>Nebulizer 20 mg/ampule</td>
<td>1 ampule tid-qid</td>
</tr>
</tbody>
</table>

Leukotriene Receptor Antagonists

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosage Form</th>
<th>Adult Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Montelukast</td>
<td>10 mg tablet</td>
<td>10 mg qhs</td>
</tr>
<tr>
<td></td>
<td>10 or 20 mg tablet</td>
<td>40 mg daily (20 mg tablet bid)</td>
</tr>
<tr>
<td>Zafirlukast</td>
<td>10 mg qhs</td>
<td></td>
</tr>
</tbody>
</table>

Methylxanthines (Serum monitoring is important [serum concentration of 5-12 mcg/mL at steady state].)

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosage Form</th>
<th>Adult Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Theophylline</td>
<td>Liquids, sustained-release tablets, and capsules</td>
<td>Starting dose 10 mg/kg/day up to 300 mg max; usual max 800 mg/day</td>
</tr>
</tbody>
</table>

DPI, dry powder inhaler; MDI, metered-dose inhaler.

*Adapted from EPR—Update 2002.

Notes:
- The most important determinant of appropriate dosing is the clinician’s judgment of the patient's response to therapy.
- Some doses may be outside package labeling, especially in the high-dose range.

**Estimated Comparative Daily Dosages for Inhaled Corticosteroids**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adult Low Daily Dose</th>
<th>Adult Medium Daily Dose</th>
<th>Adult High Daily Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beclomethasone CFC</td>
<td>168–504 mcg</td>
<td>504–840 mcg</td>
<td>&gt;840 mcg</td>
</tr>
<tr>
<td>Beclomethasone H FA</td>
<td>80–240 mcg</td>
<td>240–480 mcg</td>
<td>&gt;480 mcg</td>
</tr>
<tr>
<td>Budesonide DPI</td>
<td>200–600 mcg</td>
<td>600–1,200 mcg</td>
<td>&gt;1,200 mcg</td>
</tr>
<tr>
<td>Flunisolide</td>
<td>500–1,000 mcg</td>
<td>1,000–2,000 mcg</td>
<td>&gt;2,000 mcg</td>
</tr>
<tr>
<td>Fluticasone</td>
<td>88–264 mcg</td>
<td>264–660 mcg</td>
<td>&gt;660 mcg</td>
</tr>
<tr>
<td>M DI: 44, 110, or 220 mcg/puff</td>
<td>300–750 mcg</td>
<td>300–750 mcg</td>
<td>&gt;750 mcg</td>
</tr>
<tr>
<td>Triamcinolone acetonide</td>
<td>400–1,000 mcg</td>
<td>1,000–2,000 mcg</td>
<td>&gt;2,000 mcg</td>
</tr>
</tbody>
</table>

DPI, dry powder inhaler; M DI, metered-dose inhaler.

*Adapted from EPR—Update 2002.
Manage Asthma Exacerbations During Pregnancy and Lactation: Home Treatment

**Assess Severity**
- Measure PEF: Value <50% personal best or predicted suggests severe exacerbation.
- Note signs and symptoms: Degrees of cough, breathlessness, wheeze, and chest tightness correlate imperfectly with severity of exacerbation.
- Accessory muscle use and suprasternal retractions suggest severe exacerbation.
- Note presence of fetal activity*

**Initial Treatment**
- Short-acting inhaled beta_2_-agonist: up to 3 treatments of 2–4 puffs by MDI at 20-minute intervals or single nebulizer treatment.

**Good Response**
**Mild Exacerbation**
- PEF >80% predicted or personal best.
- No wheezing or shortness of breath.
- Response to short-acting inhaled beta_2_-agonist sustained for 4 hours.
- Appropriate fetal activity.*

**Treatment:**
- May continue short-acting inhaled beta_2_-agonist every 3–4 hours for 24–48 hours.
- For patients on inhaled corticosteroid, double dose for 7–10 days.

**Contact clinician for followup instructions.**

**Incomplete Response**
**Moderate Exacerbation**
- PEF 50%–80% predicted or personal best.
- Persistent wheezing and shortness of breath.
- Decreased fetal activity.*

**Treatment:**
- Add oral corticosteroid.
- Continue short-acting inhaled beta_2_-agonist.

**Contact clinician urgently (this day) for instructions.**

**Poor Response**
**Severe Exacerbation**
- PEF <50% predicted or personal best.
- Marked wheezing and shortness of breath.
- Decreased fetal activity.*

**Treatment:**
- Add oral corticosteroid.
- Repeat short-acting inhaled beta_2_-agonist immediately.
- If distress is severe and nonresponsive, call your clinician immediately and proceed to emergency department; consider calling ambulance or 911.

**Proceed to emergency department.**

MDI, metered-dose inhaler; PEF, peak expiratory flow.
*Fetal activity is monitored by observing whether fetal kick counts decrease over time.
**Management of Asthma Exacerbations During Pregnancy and Lactation: Emergency Department and Hospital-Based Care**

**Initial Assessment**
- History, physical examination (auscultation, use of accessory muscles, heart rate, respiratory rate), PEF or FEV₁, oxygen saturation, and other tests as indicated
- Initiate fetal assessment (consider continuous electronic fetal monitoring and/or biophysical profile if pregnancy has reached fetal viability)

**FEV₁ or PEF >50%**
- Short-acting inhaled beta₂-agonist by MDI or nebulizer, up to three doses in first hour
- Oxygen to achieve O₂ saturation ≥95%
- Oral systemic corticosteroid if no immediate response or if patient recently took oral systemic corticosteroid

**FEV₁ or PEF <50% (Severe Exacerbation)**
- High-dose short-acting inhaled beta₂-agonist by nebulization every 20 minutes or continuously for 1 hour plus inhaled ipratropium bromide
- Oxygen to achieve O₂ saturation >95%
- Oral systemic corticosteroid

**Impending or Actual Respiratory Arrest**
- Intubation and mechanical ventilation with 100% O₂
- Nebulized short-acting inhaled beta₂-agonist plus inhaled ipratropium bromide
- Intravenous corticosteroid

**Repeat Assessment**
- Symptoms, physical examination, PEF, O₂ saturation, other tests as needed
- Continue fetal assessment

**Moderate Exacerbation**
- FEV₁ or PEF 50%–80% predicted/personal best
- Physical exam: moderate symptoms
  - Short-acting inhaled beta₂-agonist every 60 minutes
  - Systemic corticosteroid
  - Oxygen to maintain O₂ saturation >95%
  - Continue treatment 1–3 hours, provided there is improvement

**Severe Exacerbation**
- FEV₁ or PEF <50% predicted/personal best
- Physical exam: severe symptoms at rest, accessory muscle use, chest retraction
- History: high-risk patient
- No improvement after initial treatment
  - Short-acting inhaled beta₂-agonist hourly or continuously plus inhaled ipratropium bromide
  - Oxygen
  - Systemic corticosteroid

**Improvement**

**Good Response**
- FEV₁ or PEF ≥70%
- Response sustained 60 minutes after last treatment
- No distress
- Physical exam: normal
- Reassuring fetal status

**Incomplete Response**
- FEV₁ or PEF >50% but <70%
- Mild or moderate symptoms
- Continue fetal assessment

**Poor Response**
- FEV₁ or PEF <50%
- PCO₂ >42 mmHg
- Physical exam: symptoms severe, drowsiness, confusion
- Continue fetal assessment

**Individualized Decision re: Hospitalization**

**Discharge Home**
- Continue treatment with short-acting inhaled beta₂-agonist
- Continue course of oral systemic corticosteroid
- Initiate or continue inhaled corticosteroid until review at medical followup
- Patient education
  - Review medicine use
  - Review/initiate action plan
  - Recommend close medical followup

**Admit to Hospital Ward**
- Short-acting inhaled beta₂-agonist plus inhaled ipratropium bromide
- Systemic (oral or intravenous) corticosteroid
- Oxygen
- Monitor FEV₁ or PEF, O₂ saturation, pulse
- Continue fetal assessment until patient stabilized

**Admit to Hospital Intensive Care**
- Short-acting inhaled beta₂-agonist hourly or continuously plus inhaled ipratropium bromide
- Intravenous corticosteroid
- Oxygen
- Possible intubation and mechanical ventilation
- Continue fetal assessment until patient stabilized

**Discharge Home**
- Continue treatment with short-acting inhaled beta₂-agonist
- Continue course of oral systemic corticosteroid
- Initiate or continue inhaled corticosteroid until review at medical followup
- Patient education
  - Review medicine use
  - Review/initiate action plan
  - Recommend close medical followup

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FEV₁, forced expiratory volume in 1 second; MDI, metered-dose inhaler; PCO₂, carbon dioxide partial pressure; PEF, peak expiratory flow.

*Adapted from EPR-2 1997.
### Medications and Dosages for Asthma Exacerbations During Pregnancy and Lactation

<table>
<thead>
<tr>
<th>Medications</th>
<th>Adult Dose</th>
<th>Child Dose</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Short-Acting Inhaled Beta2-Agonists</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albuterol</td>
<td>2.5–5 mg every 20 minutes for 3 doses, then 2.5–10 mg every 1–4 hours as needed, or 0.15 mg/kg (minimum dose 2.5 mg) every 20 minutes for 3 doses, then 0.15–0.3 mg/kg up to 10 mg every 1–4 hours as needed, or 0.5 mg/kg/hour by continuous nebulization</td>
<td>0.15 mg/kg (minimum dose 2.5 mg) every 20 minutes for 3 doses, then 0.15–0.3 mg/kg up to 10 mg every 1–4 hours as needed, or 0.5 mg/kg/hour by continuous nebulization</td>
<td>Only selective beta2-agonists are recommended. For optimal delivery, dilute aerosols to minimum of 3 mL at gas flow of 6–8 L/min. As effective as nebulized therapy if patient is able to coordinate.</td>
</tr>
<tr>
<td>M Dl (90 mcg/puff)</td>
<td>4–8 puffs every 20 minutes up to 4 hours, then every 1–4 hours as needed</td>
<td>4–8 puffs every 20 minutes for 3 doses, then every 1–4 hours inhalation maneuver; use spacer/holding chamber</td>
<td></td>
</tr>
<tr>
<td>Bitotlerol</td>
<td>See albuterol dose.</td>
<td>See albuterol dose.</td>
<td>HAs not been studied in severe asthma exacerbations. Do not mix with other drugs.</td>
</tr>
<tr>
<td>M Dl (370 mcg/puff)</td>
<td>See albuterol dose.</td>
<td>See albuterol dose.</td>
<td>HAs not been studied in severe asthma exacerbations.</td>
</tr>
<tr>
<td>Levalbuterol (R-albuterol)</td>
<td>1.25–2.5 mg every 20 minutes for 3 doses, then 1.25–5 mg every 1–4 hours as needed, or 0.075 mg/kg (minimum dose 1.25 mg) every 20 minutes for 3 doses, then 0.075–0.15 mg/kg up to 5 mg every 1–4 hours as needed, or 0.25 mg/kg/hour by continuous nebulization</td>
<td>0.075 mg/kg (minimum dose 1.25 mg) every 20 minutes for 3 doses, then 0.075–0.15 mg/kg up to 5 mg every 1–4 hours as needed, or 0.25 mg/kg/hour by continuous nebulization</td>
<td>0.63 mg of levalbuterol is equivalent to 1.25 mg of racemic albuterol for both efficacy and side effects.</td>
</tr>
<tr>
<td>Pirbuterol</td>
<td>See albuterol dose.</td>
<td>See albuterol dose.</td>
<td>HAs not been studied in severe asthma exacerbations.</td>
</tr>
<tr>
<td>M Dl (200 mcg/puff)</td>
<td>See albuterol dose; thought to be half as potent as albuterol on a mg basis.</td>
<td></td>
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</tr>
<tr>
<td><strong>Systemic (Injected) Beta2-Agonists</strong></td>
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<tr>
<td>Epinephrine</td>
<td>0.3–0.5 mg every 20 minutes for 3 doses sq</td>
<td>0.01 mg/kg up to 0.3–0.5 mg every 20 minutes for 3 doses sq</td>
<td>No proven advantage of systemic therapy over aerosol.</td>
</tr>
<tr>
<td>Terbutaline (1 mg/mL)</td>
<td>0.25 mg every 20 minutes for 3 doses sq</td>
<td>0.01 mg/kg every 20 minutes for 3 doses, then every 2–6 hours as needed sq</td>
<td>No proven advantage of systemic therapy over aerosol.</td>
</tr>
<tr>
<td><strong>Anticholinergics</strong></td>
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</tr>
<tr>
<td>Ipratropium bromide</td>
<td>0.5 mg every 30 minutes for 3 doses, then every 2–4 hours as needed</td>
<td>0.25 mg every 20 minutes for 3 doses, then every 2–4 hours</td>
<td>M ay mix in same nebulizer with albuterol. Should not be used as first-line therapy; should be added to beta2-agonist therapy. Dose delivered from M Dl is low and has not been studied in asthma exacerbations.</td>
</tr>
<tr>
<td>M Dl (18 mcg/puff)</td>
<td>4–8 puffs as needed</td>
<td>4–8 puffs as needed</td>
<td></td>
</tr>
<tr>
<td>Ipratropium with albuterol</td>
<td>3 mL every 30 minutes for 3 doses, then every 2–4 hours as needed</td>
<td>1.5 mL every 20 minutes for 3 doses, then every 2–4 hours</td>
<td>Contains EDTA to prevent discoloration. This additive does not induce bronchospasm.</td>
</tr>
<tr>
<td>M Dl (Each puff contains 18 mcg ipratropium bromide and 90 mcg albuterol)</td>
<td>4–8 puffs as needed</td>
<td>4–8 puffs as needed</td>
<td></td>
</tr>
<tr>
<td><strong>Systemic Corticosteroids</strong></td>
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</tbody>
</table>

(Dosages and comments apply to all three corticosteroids)

### Notes:
- Adapted from EPR—Update 2002.
- The most important determinant of appropriate dosing is the clinician’s judgment of the patient’s response to therapy.
- A medication is selected based on the physician’s judgment of the patient’s response to therapy and additional factors such as the patient’s gestational age, complications, coinfections, concomitant medications, and personal and maternal preferences.
- The most commonly used corticosteroids are Prednisone and Methylprednisolone.
- For outpatient “burst” use 40–60 mg in single or 2 divided doses for adults (children: 1–2 mg/kg/day, maximum 60 mg/day) for 3–10 days.
Summary of Control Measures for Environmental Factors That Can Make Asthma Worse

Allergens:
Reduce or eliminate exposure to the allergen(s) the patient is sensitive to, including:

- **Animal dander**: Remove animal from house, or, at a minimum, keep animal out of patient's bedroom and seal or cover with a filter the air ducts that lead to the bedroom.

- **House-dust mites**:
  - Essential: Encase mattress in an allergen-impermeable cover; encase pillow in an allergen-impermeable cover or wash it weekly; wash sheets and blankets on the patient's bed in hot water weekly (water temperature of >130°F is necessary for killing mites).
  - Desirable: Reduce indoor humidity to less than 50 percent; remove carpets from the bedroom; avoid sleeping or lying on upholstered furniture; remove carpets that are laid on concrete.

- **Cockroaches**: Use poison bait or traps to control. Do not leave food or garbage exposed.

- **Pollens** (from trees, grass, or weeds) and outdoor molds: To avoid exposure, adults should stay indoors—especially during the afternoon—with the windows closed during the season in which they have problems with outdoor allergens.

- **Indoor mold**: Fix all leaks and eliminate water sources associated with mold growth; clean moldy surfaces. Consider reducing indoor humidity to less than 50 percent.

Tobacco Smoke:
Advise patients and others in the home who smoke to stop smoking or to smoke outside the home. Discuss ways to reduce exposure to other sources of tobacco smoke, such as from daycare providers and the workplace.

Indoor/Outdoor Pollutants and Irritants:
Discuss ways to reduce exposures to the following:

- Wood-burning stoves or fireplaces
- Unvented stoves or heaters
- Other irritants (e.g., perfumes, cleaning agents, sprays)

*Adapted from EPR-2 1997.

**REFERENCES**


