

Understanding Asthma Medications

Long-Term Control Medications Used to Treat Asthma

Long-term control medications are taken daily on a long-term basis to achieve and maintain control of persistent asthma.

Inhaled corticosteroids

The most potent and consistently effective long-term anti-inflammatory medications for asthma, with fewer side effects than oral corticosteroids. Used for management of persistent asthma at all levels of severity to improve symptoms and pulmonary function.

What are the names of some commonly prescribed inhaled corticosteroids?

Advair®, Aerobid®, Azmacort®, Flovent®, Pulmicort® and Vanceril®

When is it used?

- Long-term prevention of symptoms; controls, reverses and keeps inflammation down.
- Reduce the need for quick-relief medications.

How does it work?

- Anti-inflammatory. Blocks late reaction to allergen and reduces airway sensitivity. Inhibit cytokine production, adhesion protein activation, and inflammatory cell migration and activation at the cellular level.
- Reverse β_2 -receptor down-regulation. Inhibit microvascular leakage.

Possible side effects:

- Cough, voice changes, oral thrush (candidiasis)
- In high doses systemic effects may occur, although studies have not proven this, and clinical significance of these effects has not been established (e.g., adrenal suppression, osteoporosis, growth suppression, and skin thinning and easy bruising).
- Some studies of inhaled corticosteroids to treat asthma in pre-pubertal children have identified growth delay or suppression that appears to be dose-dependent; others have not. The potential small risk of adverse effects on linear growth is well balanced by efficacy. The clinical significance of the findings is unclear at this time. Monitoring growth is recommended.

Other information about using this type of medication:

- Available as MDI and dry power inhaler (DPI).
- Spacer/valved-holding chamber devices with MDIs and mouth washing after inhalation decreases the risk of oral side effects and systemic absorption.
- Preparations are not absolutely interchangeable on a mcg or per puff basis. New delivery devices may provide greater delivery to air ways, which may affect dose.
- The risks of uncontrolled asthma should be weighed against the limited risks of inhaled corticosteroids. The possible but small risk of harmful effects is well balanced by their value in controlling asthma.

Long-acting β_2 -agonists

Used together with anti-inflammatory medications for long-term control of asthma symptoms. **Should not replace anti-inflammatory medications. Not to be used to treat acute symptoms or flare-ups.**

What are the names of some commonly prescribed long-acting β_2 -agonists?

Serevent®, Foradil®

When is it used?

- To improve symptoms and reduce need for quick-relief medication.
- For long-term control of symptoms, especially nighttime symptoms.
- To prevent exercise-induced bronchospasm. However, in some patients this effect may be reduced when used daily as continuous therapy. The clinical significance of this finding is unclear.

How does it work?

- Starts working slower but lasts longer than short-acting β_2 -agonists.
- May get better symptom control when added to standard doses of inhaled corticosteroids instead of just increasing the corticosteroid dose.
- Bronchodilation: relax bronchial smooth muscle following adenylate cyclase activation and increase in cyclic AMP producing functional antagonism of bronchoconstriction at the cellular level.
- In vitro, inhibit mast cell mediator release, decrease vascular permeability, and increase mucociliary clearance.

Possible side effects:

- Increased heart rate, shakiness, hypokalemia, prolongation of QTc interval in overdose.
- A diminished bronchoprotective effect may occur within 1 week of chronic therapy. Clinical significance has not been established.

Other information about using this type of medication:

- Available as metered-dose inhaler (MDI), dry powder inhaler (DPI), Diskus®, and tablets. Inhaled long-acting β_2 -agonists are preferred because they are longer acting and have fewer side effects than time-release pills.
- Should not replace anti-inflammatory medications.
- Not to be used to treat acute symptoms or flare-ups.
- Clinical significance of potentially developing tolerance is not clear because studies show symptom control and bronchodilation are maintained.
- May provide better symptom control when added to standard doses of inhaled corticosteroid instead of increasing the corticosteroid dosage.

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Leukotriene modifiers

May be considered an alternative therapy to low doses of inhaled corticosteroids, cromolyn or nedocromil for patients with mild or moderate persistent asthma.

What are the names of some commonly prescribed leukotriene modifiers?

Accolate®, Singulair®, and Zyflo®

When is it used?

- May be considered as alternative therapy to low doses if inhaled corticosteroids for patients with mild persistent asthma, but the position of leukotriene modifiers in therapy has not been fully established. Some studies suggest that leukotriene modifiers may be effective when added to inhaled corticosteroids in the management of moderate persistent asthma (step 3) and when given the night before exercise to prevent exercise-induced bronchospasm.
- Improve symptoms and pulmonary function.
- Reduce the need for quick-relief medications.

How does it work?

- Leukotriene receptor antagonists (e.g. montelukast, zafirlukast) block LTD₄ receptors; 5-lipoxygenase inhibitors (e.g. zileuton) block synthesis of all leukotrienes at the cellular level.

Possible side effects:

- Elevations of liver enzymes have been reported with zileuton in some patients. Monitoring is recommended.
- In rare cases, adult patients have presented with systemic eosinophilia and vasculitis with clinical features consistent with Churg Strauss syndrome. These events usually have been associated with reducing oral corticosteroid therapy while initiating a leukotriene modifier therapy. No causal relationship has been established.

Other information about using this type of medication:

- Available as tablets. Tablets should be taken at least 1 hour before or 2 hours after meals for optimum effects.
- Zafirlukast inhibits the metabolism of warfarin and increases prothrombin time; it is a competitive inhibitor of the CYP2C9 hepatic microsomal isozymes. (It has not affected elimination of terfenadine, theophylline, or ethinyl estradiol drugs metabolized by the CYP3A4 isozymes.)
- Zileuton is microsomal CYP3A4 enzyme inhibitor that can inhibit the metabolism of terfenadine, theophylline, and warfarin. Doses of these drugs should be monitored accordingly. Hepatic enzymes (ALT) should also be monitored.

Oral corticosteroids

Often used to gain prompt control of poorly controlled persistent asthma, or when starting long-term therapy.

What are the names of some commonly prescribed oral corticosteroids?

Deltasone®, Prednisone®

When is it used?

- For short-term (3-10 days) “burst”, broad anti-inflammatory effects.
- For long-term prevention of symptoms in severe persistent asthma; controls, reverses and keeps inflammation down.

How does it work?

- Anti-inflammatory. Blocks late reaction to allergen and reduce airway sensitivity. Inhibits cytokine production, adhesion protein activation, and inflammatory cell migration and activation at the cellular level.
- Reverse β_2 -receptor down-regulation. Inhibit microvascular leakage.

Possible side effects:

- Short-term use: reversible, abnormalities in sugar metabolism, increased appetite, fluid retention, weight gain, mood change, high blood pressure, peptic ulcer, and rarely aseptic necrosis of femur.
- Long-term use is associated with systemic effects: adrenal axis suppression, growth suppression, dermal thinning, hypertension, diabetes, Cushing’s syndrome, cataracts, muscle weakness, and – in rare cases – impaired immune function.
- Consideration should be given to coexisting conditions that could be worsened by systemic corticosteroids, such as herpes virus infections, varicella, tuberculosis, hypertension, peptic ulcer, and Strongyloides.

Other information about using this type of medication:

- Use at lowest effective dose.
- For long-term use in severe persistent asthma, fewer harmful effects have been seen with every-other-day morning dosing.

Cromolyn Sodium/Nedocromil Sodium

Mild to moderate anti-inflammatory medications. Alternative therapy to low-doses of inhaled corticosteroids in mild persistent asthma.

What are the names of some commonly prescribed cromolyn sodium/nedocromil medications?

Intal®, Tilade®

When is it used?

- May be used as first choice for long-term-control therapy for children.
- Nedocromil may also be added to inhaled corticosteroids in moderate asthma.

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- Can also be used as preventive treatment prior to exercise or unavoidable exposure to known allergens (cold air, exercise, allergens) on an as-needed basis.
- To improve symptoms and pulmonary function.
- To reduce the need for quick-relief medications.

How does it work?

- Anti-inflammatory: Block early and late reaction to allergen. Interfere with chloride channel function at the cellular level. Stabilize mast cell membranes and inhibit activation and release of mediators from eosinophils and epithelial cells (which cause swelling).
- Inhibit acute response to exercise, cold dry air, and SO₂.

Possible side effects:

- 15 to 20 percent of patients complain of an unpleasant taste from nedocromil.

Other information about using this type of medication:

- Available as metered-dose inhaler (MDI). Cromolyn sodium is also available as nebulizer solution. Both are considered very safe.
- Therapeutic response to cromolyn and nedocromil often occurs within 2 weeks, but a 4 to 6 week trial may be needed to determine maximum benefit.
- Dose of cromolyn MDI (1 mg/puff) may not be enough to change airway sensitivity. Nebulizer delivery (20 mg/ampule) may be better for some patients.

Methylxanthines (theophylline)

Used as add-on therapy to anti-inflammatory medications for long-term control of asthma symptoms, especially nighttime symptoms.

What are the names of some commonly prescribed methylxanthines?

Theolair®, Theodur®

When is it used?

- Long-term control and prevention of symptoms, especially nocturnal symptoms.
- Produces mild to moderate bronchodilation.
- Theophylline is an alternative, but not preferred, therapy for persistent asthma.

How does it work?

- Bronchodilation: Smooth muscle relaxation from phosphodiesterase inhibition and possibly adenosine antagonism (to open up the airways).
- May affect eosinophilic infiltration into bronchial mucosa as well as decrease T-lymphocyte numbers in epithelium (to slow mucus production).
- Increases diaphragm contractility and mucociliary clearance (to clear mucus from airways).

Possible side effects:

- Side effects at usual therapeutic doses include stomach upset, difficulty in urination in elderly males with prostate disease, sleeplessness, and hyperactivity in some children.
- Dose-related acute toxicities include increased heart rate, nausea and vomiting, irregular heart beats (SVT), central nervous system stimulation, headache, seizures, vomiting blood, high blood sugar, and hypokalemia.
- Side effects increase with increasing levels of the medication in the body. In some children, side effects may occur with lower levels of the medication in the body.

Other information about using this type of medication:

- Available as time-release pills and capsules.
- Monitoring is required to maintain serum levels between 5 and 15 mcg/mL. Viral illnesses with fever, age, certain medications (e.g. erythromycin), and diet can increase absorption and bioavailability, which can increase levels of the medication in the body.
- Not generally recommended for asthma flare-ups. There is little proof of added benefit to optimal doses of inhaled b₂-agonists. Blood concentration of this drug must be monitored closely.

Adapted from the Guidelines for the Diagnosis and Management of Asthma, National Asthma Education and Prevention Program, National Institutes of Health, 1997

Quick-relief Medications Used to Treat Asthma

Quick-relief medications give fast relief for tight, narrowed airways and the symptoms of coughing, wheezing, and chest tightness that happen with asthma.

Short-acting b₂-agonists

Inhaled short-acting b₂-agonists are the drug of choice for treating acute asthma symptoms and attacks, or flare-ups.

What are the names of some commonly prescribed short-acting b₂-agonists?

Albuterol®, Brethine®, Proventil®, Xopenex®

When is it used?

- For relief of acute symptoms and prevent exercise-induced bronchospasm.

How does it work?

- Bronchodilation: relax bronchial smooth muscle following adenylate cyclase activation and increase in cyclic AMP producing functional antagonism of bronchoconstriction, usually within 5 to 10 minutes of administration (opens up the airways by working on a cellular level).

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Possible side effects:

- Increased heart rate, shakiness, hypokalemia, increased lactic acid, headache, high blood sugar. Inhaled route, in general, causes few side effects.
- Patients who already have heart disease, especially the elderly, may have harmful cardiovascular reactions with inhaled therapy.

Other information about using this type of medication:

- Inhaled route starts working faster, has fewer side effects, and works better than oral medication. The less β_2 -selective agents (isoproterenol, metaproterenol, isoetharine, and epinephrine) are not recommended due to their potential for excessive cardiac stimulation, especially in high doses. Albuterol liquid is not recommended.
- For patients with mild intermittent asthma, regularly scheduled daily use neither harms nor benefits asthma control. Regularly scheduled daily use is not generally recommended.
- If the medication does not seem to be working, or if it needs to be used too often (more than 1 canister/month) means that the asthma is not under control, and a doctor needs to evaluate and possibly increase (or start) long-term control therapy. Use of greater than 2 canisters/month poses additional adverse risks.

Oral (systemic) corticosteroids

Used for moderate-to-severe exacerbations to speed recovery and prevent recurrence of exacerbations.

What are the names of some commonly prescribed oral (systemic) corticosteroids?

Deltasone®, Prednisone®

When is it used?

- Usually requires short-term (3-10 days) "burst", broad anti-inflammatory effects.
- Broad anti-inflammatory effects- to stop an asthma flare-up, reverse inflammation, speed recovery and reduce rate of relapse.

How does it work?

- Anti-inflammatory. Blocks late reaction to allergen and reduce airway sensitivity. Inhibit cytokine production, adhesion protein activation, and inflammatory cell migration and activation at the cellular level.
- Reverse β_2 -receptor down-regulation. Inhibit microvascular leakage.

Possible side effects:

- Short-term use: reversible changes in sugar metabolism, increased appetite, fluid retention, weight gain, mood alteration, hypertension, peptic ulcer, and rarely aseptic necrosis of femur.
- Consideration should be given to coexisting conditions that could be worsened by systemic corticosteroids, such as herpes virus infections, varicella, tuberculosis, hypertension, peptic ulcer, and *Strongyloides*.

Other information about using this type of medication:

- Short-term therapy should continue until patient achieves 80% Peak Expiratory Flow personal best or symptoms resolve. This usually requires 3 to 10 days, but may require longer. There is no evidence that tapering the dose following improvement prevents relapse.

Anticholinergics (ipratropium bromide)

May provide some additive benefit to inhaled β_2 -agonists in severe asthma attacks. May be an alternative bronchodilator for patients who do not tolerate inhaled β_2 -agonists.

What is the name of a commonly prescribed anticholinergic medication?

Atrovent®

When is it used?

- For relief of acute bronchospasm.

How does it work?

- Bronchodilation. Competitive inhibition of muscarinic cholinergic receptors (opens the airways by working at the cellular level).
- Reduces intrinsic vagal tone to the airways. May block reflex bronchoconstriction secondary to irritants or to reflux esophagitis.
- May decrease mucus gland secretion (so body makes less mucus).

Possible side effects:

- Drying of mouth and respiratory secretions, increased wheezing in some people, blurred vision if sprayed in eyes.

Other information about using this type of medication:

- Reverses only cholinergically mediated bronchospasm; does not modify reaction to antigen. Does not block exercise-induced bronchospasm.
- May provide additive effects to β_2 -agonist but has slower onset of action.
- Is an alternative for patients with intolerance to β_2 -agonists.
- Treatment of choice for bronchospasm due to beta-blocker medication.

Adapted from the Guidelines for the Diagnosis and Management of Asthma, National Asthma Education and Prevention Program, National Institutes of Health, 1997

Over-the-Counter Medications

NOTE: Over-the-counter asthma medications do not contain the same ingredients as prescribed asthma medications. They have many more side effects, and may actually worsen asthma symptoms.