

Montelukast and Zafirlukast: Leukotriene Receptors Antagonists

Montelukast and Zafirlukast are **Cysteinyl Leukotriene Receptor Antagonists (LTRAs)** used in the **prophylactic treatment of asthma** , particularly when triggered by **antigens, exercise, or drugs (e.g., aspirin)** .

Classification of Leukotriene Modulators

Class	Example	Mechanism
5-Lipoxygenase Inhibitor	Zileuton	Inhibits leukotriene synthesis
Cysteinyl Leukotriene Receptor Antagonists (CysLT1)	Montelukast, Zafirlukast	Blocks receptor binding of LTC ₄ , LTD ₄ , and LTE ₄

What Are Leukotrienes?

- **Fatty acid-derived eicosanoids** formed from **arachidonic acid** via the **5-lipoxygenase** enzyme pathway.
- Released by **mast cells, eosinophils** , and **basophils** upon allergen exposure.
- Mediate **bronchoconstriction, vascular permeability (edema)** , and **eosinophil recruitment** .

Types

- **LTB₄** : Strong **chemoattractant** , promotes neutrophil migration.
- **LTC₄, LTD₄, LTE₄** (Cysteinyl leukotrienes): Mediate **bronchospasm** , **mucosal edema** , and **eosinophilic inflammation** .

Montelukast

- **Chemical Class** : Leukotriene Receptor Antagonist
- **Therapeutic Class** : Antiasthmatic
- **Pregnancy Category** : B
- **Bioavailability** : >90%
- **Protein Binding** : ~99%
- **Half-life** : ~2.7–5.5 hours
- **Metabolism** : Liver (CYP3A4, CYP2C9)
- **Excretion** : Biliary

Mechanism of Action

Blocks **CysLT1 receptors** ? prevents actions of LTC₄, LTD₄, LTE₄ ? reduces

bronchoconstriction, inflammation, and edema .

Indications

Condition	Dose
Asthma prophylaxis	10 mg once daily (evening)
Exercise-induced bronchoconstriction	10 mg, 2 hrs before activity
Allergic rhinitis	10 mg once daily
Pediatric dosing	12–24 mo: 4 mg granules 2–5 yrs: 4 mg chewable 6–14 yrs: 5 mg chewable >15 yrs: Adult dose

Zafirlukast

- **Use** : Maintenance treatment of asthma
- **Dose** : 20 mg **twice daily** (adults), 10 mg **twice daily** (ages 5–12)
- **Administration** : Take **1 hour before or 2 hours after meals** for optimal absorption.

Clinical Pharmacology

- Not a bronchodilator for acute asthma attacks.
- Used **as add-on therapy** in patients not controlled on **inhaled corticosteroids** and short-acting β_2 -agonists.

Adverse Effects

Montelukast & Zafirlukast

- **Common** : Headache, abdominal pain, fatigue, fever
- **Neuropsychiatric** : Agitation, depression, insomnia, suicidal ideation, hallucinations (especially Montelukast – black box warning)
- **Respiratory** : Cough, pharyngitis, sinusitis
- **GI** : Diarrhea, liver enzyme elevation (esp. Zafirlukast)
- **Rare** : Churg-Strauss syndrome (eosinophilic vasculitis), hypersensitivity reactions, hepatotoxicity, Stevens-Johnson syndrome

Drug Interactions

Drug	Effect
Phenobarbital	? Montelukast levels (enzyme inducer)
Warfarin	? Prothrombin time (Zafirlukast)
Erythromycin	? Zafirlukast absorption
Theophylline	? Plasma levels (Zafirlukast)

Warnings and Precautions

- **Not for acute asthma** or **status asthmaticus** .
- **Do not substitute abruptly for corticosteroids** .
- Monitor closely during **steroid tapering** for signs of **vasculitis (Churg-Strauss)** .
- Monitor for **neuropsychiatric symptoms** during therapy initiation and dose changes.
- **Avoid NSAIDs** in aspirin-sensitive patients; Montelukast may not prevent reactions.
- **Zafirlukast is contraindicated in pregnancy and breastfeeding** .
- **Caution** in phenylketonuria patients: Chewable forms contain phenylalanine.

Clinical Pearls

- Montelukast is especially beneficial in:
 - **Aspirin-sensitive asthma**
 - **Exercise-induced bronchospasm**
 - **Children with persistent asthma**
- **Evening administration** preferred for maximum symptom control.
- Monitor **liver function** periodically, especially with Zafirlukast.