

# Drugs for airway disease

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## Abstract

Asthma is a heterogeneous disease characterized by chronic airway inflammation and variable expiratory airflow limitation. It affects 5–15% of people worldwide and shows an increasing prevalence over the last decade. The treatment of asthma is well established in current guidelines, with the aim of achieving optimal disease control and preventing acute exacerbations using a stepwise medication approach. Drugs are commonly divided into ‘relievers’, which quickly alleviate airway obstruction, and ‘controllers’, which suppress the pathophysiology and provide long-term symptom control.  $\beta_2$ -Adrenoreceptor agonists are the most effective therapy for reversing bronchial obstruction. Inhaled corticosteroids are recommended as first-line ‘controller’ therapy for persistent asthma. Acute exacerbations often require systemic corticosteroids. Muscarinic antagonists, methylxanthines, anti-leukotrienes, cromones and macrolides also play a key role in disease management. The use of biological agents has recently received increasing attention, prompting a drive for a so-called ‘precision-based medicine’ approach, particularly in more severe disease. The only biological drug currently licensed in Europe is the anti-IgE monoclonal antibody omalizumab. Several other antibodies and targeted molecules are under advanced development and are expected to be available on prescription soon, although they will be expensive.

**Keywords**  $\beta_2$ -Agonist; adverse effect; anticholinergic; asthma; biological agent; bronchoconstriction; corticosteroid; exacerbation; inflammation; theophylline

## Introduction

Asthma is a heterogeneous disease usually characterized by chronic airway inflammation. It is defined by a history of respiratory symptoms that vary over time and in intensity, with evidence of variable expiratory airflow limitation.<sup>1</sup> Epidemiological

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## Key points

- The treatment of asthma is well established in guidelines and aims to achieve optimal disease control and prevent acute exacerbations
- Despite a significant increase in understanding asthma, recent innovations in therapy have been confined to inhaler devices and the advent of biological agents
- Asthma drugs are commonly divided into ‘relievers’ and ‘controllers’
- $\beta_2$ -Adrenoreceptor agonists are the most effective therapy to prevent and reverse acute bronchial obstruction
- Tiotropium is now recommended in the GINA document as an add-on bronchodilator treatment in steps 4 and 5 for adult asthmatic patients who experienced  $\geq 1$  severe exacerbations in the previous year
- Inhaled corticosteroids are recommended as first-line ‘controller’ therapy for all patients with persistent asthma
- Macrolide treatment for  $\geq 3$  weeks produces significant improvements in clinical symptoms, functional parameters and quality of life of asthmatic patients
- Several monoclonal antibodies and targeted biological molecules are in an advanced stage of development and are soon expected to be included in strategies for management of severe asthma
- The anti-IgE monoclonal antibody omalizumab is currently the only biological drug available for the treatment of asthma
- Patients who are refractory to conventional therapy or have co-morbidities represent an unmet need prompting patient-tailored treatment strategies

data show that asthma affects 5–15% of people worldwide, with increasing prevalence over the last few decades.<sup>2</sup>

Different asthma phenotypes have been described on the basis of clinical and functional patient characteristics (Figure 1).<sup>2</sup> Asthma has long been recognized as an inflammatory T helper type 2 cell-mediated disease, but recent findings support alternative pathophysiological mechanisms and effectors, which define distinct endotypes (Figure 2).<sup>2</sup>

Treatment is well established in national and international guidelines and aims to achieve optimal disease control and prevent acute exacerbations, using a stepwise approach to medication.<sup>1</sup> Drugs are commonly divided into ‘relievers’, which quickly alleviate airway obstruction, and ‘controllers’, which suppress the pathophysiology and provide long-term symptom control (Table 1).

Most patients have disease of mild to moderate severity and are managed in the community. However, patients who have more severe disease that is refractory to conventional therapy, have co-morbidities (rhinitis, gastro-oesophageal reflux) or have the recently described asthma–chronic obstructive pulmonary disease overlap syndrome (ACOS) are hard to treat, prompting

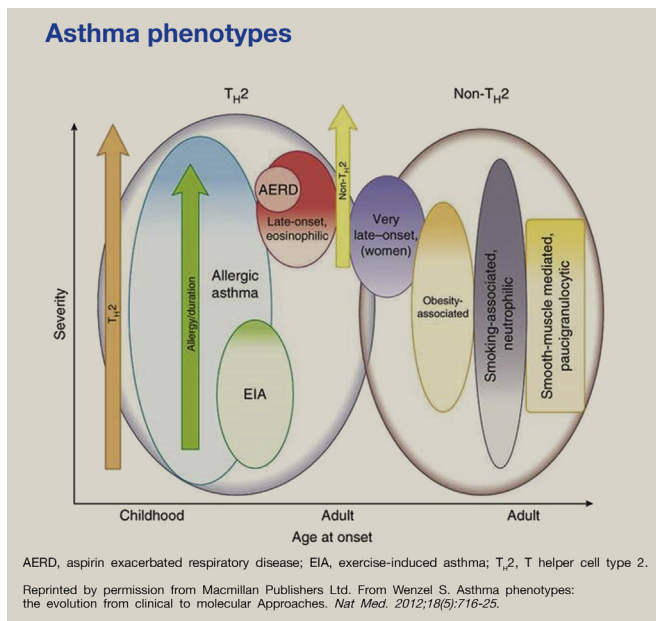


Figure 1

the current drive for a precision-based medicine approach involving patient-tailored treatment.

The following classes of drugs are relevant in the current management of asthma.

**$\beta_2$ -Adrenoreceptor agonists**

These are the mainstay of asthma management and are the most effective available treatment for preventing and reversing bronchial obstruction. Initially developed for administration as tablets, they are currently best delivered by inhalation, achieving an effective local lung effect with the least systemic toxicity. The optimal site of aerosol deposition in the lungs depends on the drug particle size, pattern of breathing and anatomy of the airways. This class of drugs includes short-acting (SABA) and long-acting (LABA)  $\beta_2$ -adrenoreceptor agonists. More recently, ultra-LABAs (indacaterol, olodaterol, vilanterol), which potentially have a once-daily dosing regimen, have been developed; however, their use is currently mainly confined to COPD.

**Mode of action**

$\beta_2$ -Adrenoreceptor agonists act via specific receptors ( $ADR\beta_2$ ), localized mainly on airway smooth muscle cells. Occupation of

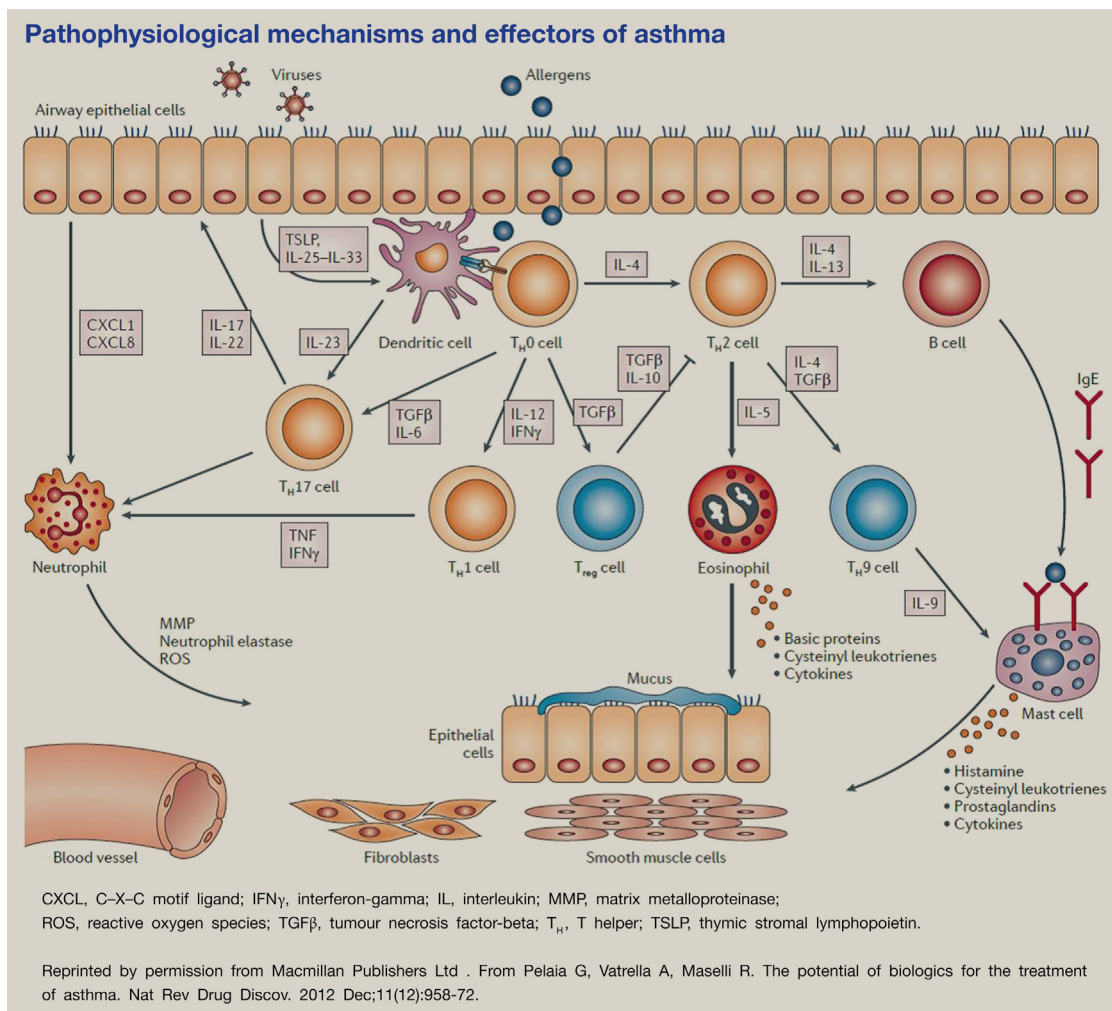


Figure 2

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