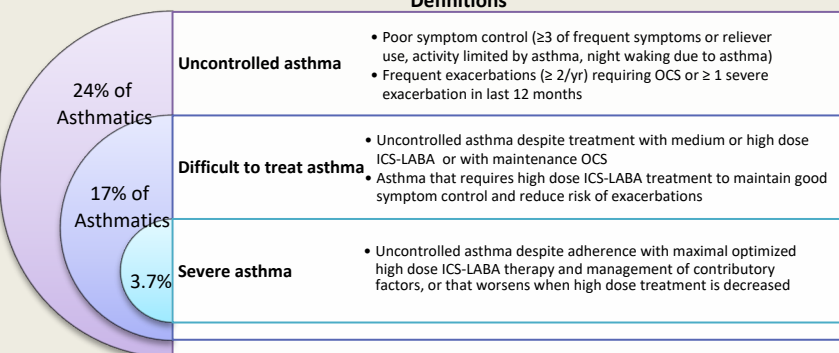


# Add-on Type 2-targeted biologic therapy for severe allergic/eosinophilic asthma

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## Definitions



## Assessment of severe asthma phenotype

- Assess factors contributing to symptoms, quality of life, and exacerbations
- Assess the severe asthma phenotype during high dose ICS treatment (or lowest possible dose of OCS)
- Investigate for comorbidities/differential diagnoses and treat as appropriate
  - Consider: FBC, CRP, IgG, IgA, IgM, IgE, fungal precipitins; CXR and/or HRCT chest; DLCO
  - Skin prick testing or specific IgE for relevant allergens, if not already done
  - Other directed testing (e.g. ANCA, CT sinuses, BNP, echocardiogram) guided by clinical picture

## Does patient have features suggestive of type 2 airway inflammation

- Blood eosinophils  $\geq 150/\mu\text{l}$  and/or
- FeNO  $\geq 20$  ppb and/or
- Sputum eosinophils  $\geq 2\%$  and/or
- Asthma is clinically **allergen-driven** and/or
- Need for maintenance **oral corticosteroids** (OCS) (Repeat peripheral eosinophils up to 3X, on lowest possible corticosteroids)

**Patient likely to have residual type 2 airway inflammation**

- Consider adherence, increasing ICS dose for 3-6 months, and co-morbidities with specific add-on treatment (AERD, ABPA, chronic rhinosinusitis, nasal polyposis, atopic dermatitis)
- THEN**
- Consider add-on Type 2-targeted biologic for patients with exacerbations or poor symptom control on high dose ICS-LABA, who:
  - have eosinophilic or allergic biomarkers, or
  - need maintenance OCS
- Consider **local hospital policy, eligibility criteria, co-morbidities and predictors of response**, as well as cost, dosing frequency, route (SC or IV), patient preference when choosing between available therapies

## Add-on anti-IgE for severe allergic asthma

**Omalizumab** is approved as add-on therapy for age  $\geq 6$  years in patients with severe allergic asthma, given by SC injections every 2-4 weeks, with dose based on weight and serum IgE. Suggested initial trial at least 4 months.

**Mechanism:** binds to Fc region of free IgE, preventing IgE binding to FcεR1 receptors, reducing free IgE and down regulating receptor expression.

### Eligibility criteria; review local institution eligibility criteria

- Positive skin test or *in vitro* reactivity to a perennial aeroallergen
- Total serum IgE and body weight within local dosing range (patients with baseline IgE lower than 76 IU/ml were less likely to experience benefit)
- Multiple documented severe asthma exacerbations despite daily high-dose ICS-LABA

### Benefits:

- RCTs in severe allergic asthma showed 34% decrease in severe exacerbations, but no significant difference in symptoms or quality of life.
- Open label studies in patients with severe allergic asthma and  $\geq 1$  severe exacerbation in last 12 mo, there was 50-65% reduction in exacerbation rate, significant improvement in quality of life and 40-50% reduction in OCS dose.

### Potential predictors of response:

- One observational study showed greater decrease in exacerbations if blood eosinophils  $\geq 260/\mu\text{l}$ , or FeNO  $\geq 20$  ppb
- Childhood-onset asthma.
- Clinical history suggesting allergen-driven asthma.
- Baseline IgE level doesn't predict likelihood of response.

**Potential adverse events;** injections site reaction, anaphylaxis in 0.2%.

## Add-on Anti-IL5 / Anti-IL5R for severe eosinophilic asthma

**Currently Approved Anti-IL5 / Anti-IL5R for ages  $\geq 12$  yrs:** Mepolizumab (Anti-IL5), 100mg given by SC injection every 4 weeks. **Benralizumab** (anti-IL5 receptor  $\alpha$  subunit), 30 mg given by SC injection 4-weekly for 3 doses then 8-weekly. **Currently Approved Anti-IL5 for ages  $\geq 18$  yrs:** Reslizumab given by IV infusion 3mg/kg 4-weekly. Suggested initial trial at least 4 months.

**Mechanism:** Interleukin-5 [IL-5] is a major regulator of eosinophilopoiesis, and eosinophil survival and activity in tissues. Benralizumab binds to IL-5 receptor  $\alpha$  subunit leading to apoptosis of eosinophils. Mepolizumab and Reslizumab bind circulating IL-5, thereby blocking its biological effects.

### Eligibility criteria; review local institution eligibility criteria for each product

- Multiple documented severe asthma exacerbations in the last year despite high dose ICS-LABA
- Blood eosinophils above locally specified level (eg  $\geq 150$  or  $\geq 300/\mu\text{l}$ ; a different threshold may apply for patients on OCS)

### Benefits:

- RCTs in severe asthma patients with exacerbations in last year, with varying eosinophil criteria, showed anti-IL5 and anti-IL5R therapy reduced severe exacerbations by ~ 55%, and improved quality of life, lung function and symptom control
- RCTs in patients taking OCS showed mepolizumab or benralizumab treatment allowed a ~ 50% reduction in median OCS dose compared to placebo
- All anti IL5 therapies reduced blood eosinophils, with almost complete suppression with benralizumab

### Potential predictors of response:

- Higher blood eosinophils (strong predictor)
- Higher number of severe exacerbations in previous year (strongly predictive)
- Adult-onset asthma
- Nasal polyposis
- Maintenance OCS at baseline

**Potential adverse events;** injections site reaction, anaphylaxis is rare. Adverse events generally similar between active and placebo groups in RCTs