UTAH SOCIETY OF
HEALTH-SYSTEM PHARMACISTS

Severe Asthma
What's Next After ICS-LABA?

Henry Bernard Best II
PGY-1 Pharmacy Practice Resident (Track B)
University of Utah Health
Bernard.Best@hsc.utah.edu
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Disclosure

- **Relevant Financial Conflicts of Interest**
  - **CE Presenter: Henry Bernard Best II, PharmD:** None
  - **CE mentor: David Young, PharmD:** None
- **Off-Label Uses of Medications**
  - None

Learning Objectives – Pharmacists

As a result of this presentation Pharmacists should be able to:

- Understand how to classify the four stages of asthma and how asthma classification applies to the therapeutic selection for a patient
- Explain the role of at least three therapeutic agents that should be considered for a patient with severe asthma before selecting a biologic agent
- Determine which patients with severe asthma are candidates for an immunomodulator and select the most appropriate biologic agent for a patient
- Compose a care plan that accounts for dosing and monitoring for a patient with severe asthma that will initiate therapy with a biologic agent

Learning Objectives – Technicians

As a result of this presentation pharmacy technicians should be able to:

- Identify the insurance requirements that must be satisfied for a patient to successfully receive a paid claim for a biologic agent
- Identify when patients are candidates for financial support from the manufacturer of a biologic agent and facilitate a patients ability receive support
- Understand when patients should receive their refills and know how to order the appropriate biologic for a patient

Terminology

- ICS: inhaled corticosteroid
- OCS: oral/systemic corticosteroid
- LABA: Long-acting beta agonist
- SABA: Short acting beta agonist
- LTRA: Leukotriene receptor antagonist
- SLIT: Sublingual Immunotherapy
- SAMA: Short-acting muscarinic agonist
- LAMA: Long-acting muscarinic agonist
- Δ Delta: "The change in"
- FEV1: amount of air exhaled in one second
- FVC: total amount of air exhaled in one breath
- FeNO: fractional exhaled nitric oxide
- TSLP: Thymic stromal lymphopoietin
- PRN: As needed
- ACQ: Asthma Control Questionnaire
- SGRQ: St. George's Respiratory Questionnaire
- AQLQ: Asthma Quality of Life Questionnaire

Asthma Statistics in the United States

Centers for Disease Control and Prevention. (2022, April 25). *Most recent asthma state data.*

Total patients (2022)	25,257,138
Severe patients (2022)	1,250,000
Asthma attacks (2019)	10,328,897
ED Visits (2019)	1,835,901
Hospitalizations (2019)	169,330
Deaths (2019)	3,524

Pathophysiology of Asthma

	Asthma Role
Lymphocytes	Initiates inflammatory cascade
Fibroblasts	Dominant source of inflammatory cytokines (Interleukin-4, Interleukin-5, etc)
Lysosomal Enzymes	Stimulate the inflammatory mediators like oxygen radicals and prostaglandins
Mast cells	These cells release of histamine and leukotrienes and cause inflammation
Eosinophils	Activate cytokines and cause inflammation
Smooth muscle contraction	Pulmonary inflammation causes narrowing of airways and shortness of breath
Leukotrienes	Airway edema, smooth muscle contraction, and increased inflammation
IgE	Serve as a defense antibody against parasitic infections and initiates an inflammatory cascade
TSLP	Induce T-helper 2 cytokine inflammation

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Asthma Prognosis

- Approximately 16% of adults newly diagnosed with asthma will experience clinical remission
- Risk factors for asthma related death
  - History of near fatal exacerbation requiring intubation or ventilator
  - Hospitalization or ER visit for asthma in last year
  - Food allergy
  - Current or recent use of oral steroids
  - Not using inhaled steroids
  - **Overuse of SABA (>1 canister in a month)**
  - Poor adherence to ICS or asthma action plan
  - Psych or psychosocial problems
  - Comorbidities (Pneumonia, diabetes, arrhythmias)

Modifiable

2022 Global Initiative for Asthma - Guidelines

Step	Step 1	Step 2	Step 3	Step 4	Step 5
Preferred Controller	PRN low dose ICS-Formoterol	PRN low dose ICS-Formoterol	Daily low dose ICS-Formoterol	Daily medium dose ICS-Formoterol	Daily high dose ICS-Formoterol LAMA Biologic
Preferred Reliever	As needed ICS-formoterol				

	Step 1	Step 2	Step 3	Step 4	Step 5
Alternate Controller	ICS when SABA taken	• Low dose ICS • LRTA • HDM SLIT	• Low dose ICS-LABA • LRTA • HDM SLIT	• Medium/high dose ICS-LABA • LAMA • LTRA • HDM SLIT	High dose ICS-LABA LAMA Biologic Azithromycin Low dose OCS
Alternate Reliever	As needed SABA				

Before every step up assess technique, adherence, and environmental exposures

Guidelines: Asthma Regimens to Avoid

Therapy	Why we should avoid
SABA only treatment regimens	Increased risk of asthma related death
Use of SAMA as alternative for SABA	Slower onset of action
Oral SABA	Adverse events
Theophylline	Adverse events
LABA without ICS	Increased risk of severe exacerbations
LAMA without ICS	Increased risk of severe exacerbations

General Rules for Escalating Therapy

- Before every step up assess technique, adherence, and environmental exposures
- For most controllers, improvement begins the day of initiation
- Full effect may take 3-4 months (Even longer in chronically uncontrolled)
- There are 3 methods of escalation:
  1. Increase the PRN ICS-formoterol
  2. Short term increase in maintenance ICS for 1-2 weeks - (Illness, allergen exposure, etc)
  3. Sustained increase for 2-3 months - (Consistently uncontrolled on previous therapy)

General Rules for De-escalating Therapy

- After 2-3 months of good control, treatment can typically be reduced without loss of control
- Continue controller treatment
- Consider risk factors (Exacerbation history, ED visits, low baseline FEV1, sputum eosinophilia)
- Baseline FeNO > 50 ppb may indicate that an exacerbation is likely when stepping down therapy

Classifying Asthma Severity

	Intermittent	Mild	Moderate	Severe
Subjective Findings	• Symptoms ≤ 2 days per week • Bedtime symptoms < 2x per month • SABA use ≤ 2 days per week • No change in daily activity	• Symptoms daily • Bedtime symptoms 3-4x per month • SABA use ≥ 2 days per week • Minor change in daily activity	• Symptoms 2-6 days per week • Bedtime symptoms 3-4x per week • SABA use daily • Noticeable change in daily activity	• Symptoms throughout the day • Bedtime symptoms 7x per week • SABA use multiple times daily • Extreme change in daily activity
Objective Findings	• FEV1: > 80% • FEV1/FVC: normal	• FEV1: ~ 80% • FEV1/FVC: normal	• FEV1: 60-80% • FEV1/FVC: Reduced by >5%	• FEV1: <60% • FEV1/FVC: Reduced by >5%
Treatment	• Step 1	• Step 2	• Step 3	• Step 4 and 5

	Step 1	Step 2	Step 3	Step 4	Step 5
Preferred Controller	As needed low dose ICS-formoterol	As needed low dose ICS-formoterol	Scheduled low dose ICS-Formoterol	Scheduled medium dose ICS-Formoterol	High dose ICS-Formoterol LAMA Biologic
Preferred Reliever	As needed low dose ICS-formoterol				

SEVERE ASTHMA

Severe Asthma – Step 5 Agents

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Alternate reliever	As needed SABA				

Severe Asthma – Step 5 Agents

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Preferred Reliever	As needed low dose ICS-formoterol				

Severe Asthma: High Dose ICS

Safety	High dose ICS-LABA Increased risk of adverse events (adrenal suppression)	
Tolerability	• Oral candidiasis (1- 6%) • Headache (7-11%) • Pharyngolaryngeal pain (6-9%) • Abdominal distress (1-7%)	• Pulmonary infection (7-8%) • Upper respiratory tract infection(4-11%) • Lower respiratory tract infection (3-8%) • Nasopharyngitis (7-11%)
Efficacy	Gina: "Increasing to high dose ICS-LABA usually provides minimal additional benefit" Adequate Trial: 3-6 months (De-escalate after) Budesonide: Attempt dosing budesonide four times daily before escalating dose	
Simplicity	ICS-Formoterol containing agents can be used at rescue agent Consider # of administrations/day	

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Preferred Reliever	As needed low dose ICS-formoterol				

Severe Asthma: High Dose ICS

ICS	ICS/LABA Example	Preparation	Directions	High Dose	Daily Puffs Required
Budesonide	Budesonide 160 mcg/formoterol 4.5 mcg	HFA	Inhale 2 puffs twice daily (Max: 12 puff/day)	>800 mcg/day	≥6
Fluticasone propionate	Fluticasone 230 mcg/salmeterol 21 mcg	Diskus	Inhale 2 puffs twice daily (Max: 4 puffs/day)	>500 mcg/day	2 to 4
	Fluticasone 500 mcg/salmeterol 50 mcg	Inhub	Inhale 1 puff twice daily (Max: 2 puffs/day)		
	Fluticasone 232 mcg/salmeterol 14 mcg	Digihaler	Inhale 1 puff twice daily (Max: 2 puffs/day)		
Fluticasone furoate	Fluticasone 200 mcg/vilanterol 25 mcg	Respiclik	Inhale 1 puff once daily (Max: 1 puff/day)	200 mcg/day	1
Mometasone	Mometasone 200 mcg/formoterol 5 mcg	Aerosol	Inhale 2 puffs twice daily (Max: 4 puffs/day)	400 mcg/day	4

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	Fluticasone 232 mcg/salmeterol 14 mcg	Digihaler	Inhale 1 puff twice daily (Max: 2 puffs/day)		
Fluticasone furoate	Fluticasone 200 mcg/vilanterol 25 mcg	Respiclik	Inhale 1 puff once daily (Max: 1 puff/day)	200 mcg/day	1
Mometasone	Mometasone 200 mcg/formoterol 5 mcg	Aerosol	Inhale 2 puffs twice daily (Max: 4 puffs/day)	400 mcg/day	4

Always consider the following when selecting an inhaler

Patient's ability to use device
Number of inhalations per day
Formoterol vs albuterol for as needed reliever
Insurance coverage

Severe Asthma

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Alternate reliever	As needed SABA				

Severe Asthma

Inflammatory phenotypes

	Step 1	Step 2	Step 3	Step 4	Step 5
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Alternate reliever	As needed SABA				

Inflammatory Asthma Phenotypes

Non-Type-2 Inflammation	
Findings	**Treatment**
• Elevated neutrophils	• LAMA • Anti IL-4R biologic • Anti TSLP biologic • Low dose azithromycin

Type-2 Inflammation (Refractory)	
Findings	**Treatment**
• Blood Eosinophils > 150 • Sputum Eosinophil ≥2% • FeNO ≥ 20 ppb • Clinically allergen-driven	• Increase ICS dose for 3-6 months • Non biologic for clinical phenotype • Biologic • OCS as last line

Severe Asthma – Step 5 Agents

	Step 1	Step 2	Step 3	Step 4	Step 5
Alternate controller	ICS when SABA taken	• Low dose ICS • LRTA • HDM SLIT	• Low dose ICS-LABA • LRTA • HDM SLIT	• Medium/high dose ICS-LABA • LAMA • LTRA • HDM SLIT	High dose ICS-LABA LAMA Biologic Azithromycin Low dose OCS
Alternate reliever	As needed SABA				

Severe Asthma: Tiotropium

Safety	• Tiotropium capsules are for inhalation via HandiHaler device, not oral administration • Tiotropium may be confused with ipratropium		
Tolerability	Xerostomia (4% to 16%)		
Efficacy	Gina: "LAMA + medium-high dose ICS-LABA improves lung function but not symptoms. Studies indicate 17% risk reduction in exacerbations when LAMA is added"		
Price	Respimat 1.25 mcg/ACT: $153.61/gram	Respimat 2.5 mcg/ACT (per gram): $22.50/gram	HandiHaler Capsules: 18 mcg: $20.48/capsule
Simplicity	• Soft-mist inhaler directions: Inhale two 1.25 mcg puffs once daily • Combination inhalers: (beclomethasone-formoterol-glycopyrrolate) and (fluticasone furoate-vilanterol-umeclidinium) • If using a non-formoterol combination inhaler, SABA is the appropriate rescue agent		

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Alternate Reliever	As needed SABA				

Severe Asthma: Azithromycin

Safety	• Sputum check for atypical mycobacteria • Bacterial resistance • ECG at baseline and at one month of therapy
Tolerability	Diarrhea is common (Initiate at 250 mg 3 times weekly then titrate to minimize adverse effects)
Efficacy	Gina: A meta-analysis found Azithromycin reduced exacerbations for adults on medium dose ICS-LABA + eosinophilia or adults on high dose ICS-LABA
Price	$15.54 - $15.57 per 500 mg tablet
Simplicity	Dosing: Azithromycin 500 mg 3 times weekly or 250 mg once daily

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Alternate Reliever	As needed SABA				

Severe Asthma: Low Dose Oral Corticosteroids

Safety	• Adrenal Suppression • CV effects • Cushing's syndrome	• Hyperglycemia • Infection • Osteoporosis (Consider preventative therapy if OCS duration > 3 months)
Tolerability	CNS effects, GI effects, Ocular effects	
Efficacy	Gina: Evidence D	
Price	$0.16-1.50 mg/tab	
Simplicity	Less than or equal to 7.5mg/day prednisone equivalent	

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Alternate Reliever	As needed SABA				

Biologic Agents

Considerations When Starting a Biologic

What Makes a Patient a Good Candidate?	Other Logistics
• Poor asthma control despite high dose ICS-LABA • High eosinophilic biomarkers • Patient requires oral corticosteroids	• Parasitic infections have been tested for • Insurances will require step therapy • Patient preference on frequency and IV vs SC agents • Drug specific criteria for therapy (Exacerbations) • Predictors for positive outcomes

Severe Asthma: Biologics Mechanism of Action

	Asthma Role
Lymphocytes / IgE	Initiates inflammatory cascade
Fibroblasts	Dominant source of inflammatory cytokines (Interleukin-4, Interleukin-5, etc)
Lysosomal Enzymes	Stimulate the inflammatory mediators like oxygen radicals and prostaglandins
Mast cells	These cells release of histamine and leukotrienes after contact with antigens
Eosinophils	Activate cytokines and cause inflammation
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Severe Asthma: Biologics Mechanism of Action

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IgE	Serve as a defense antibody against parasitic infections and initiates an inflammatory cascade
Fibroblasts	Dominant source of inflammatory cytokines (Interleukin-5)
Fibroblasts	Dominant source of inflammatory cytokines (Interleukin-4 and Interleukin-13)
TSLP	Induce T-helper 2 cytokine inflammation

Severe Asthma: Biologics Mechanism of Action

	Asthma Role
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- **Anti-IgE (Omalizumab)**
- **Anti-IL5 and Anti-IL5R (Reslizumab, Mepolizumab, Benralizumab)**
- **Anti-IL4R and Anti-IL13 (Dupilumab)**
- **Anti-TSLP (Tezepelumab-ekko)**

Biologic	Evidence	Eligibility (Exacerbation in the last year)	Positive Predictors	Dosing	Monitoring (PFTs, hypersensitivity, and infection)
Omalizumab					
Reslizumab					
Mepolizumab					
Benralizumab					
Dupilumab					
Tezepelumab -ekko					

Severe Asthma: Omalizumab vs Placebo

Objective	Evaluate the efficacy and safety of omalizumab in uncontrolled severe asthma patients receiving high-dose ICS-LABAs	
Methods	**Intervention:** Omalizumab or Placebo added to high dose ICS-LABA for 48 weeks	
	Inclusion: • Age 12-75 • Severe asthma for at least 1 year • An exacerbation in the past year	**Exclusion**: • Exacerbation requiring intubation • Oral steroids • Lung condition other than asthma
Results	**Efficacy: (Omalizumab vs Placebo)** • Rate of asthma exacerbations: 25% reduction (0.66 vs. 0.88 per patient P = 0.006) • Change in AQLQ(S) scores: +1.15 vs. +0.92 (mean difference +0.29 points [CI, 0.15 to 0.43]) • Reduced mean daily albuterol puffs: -1.58 vs. -1.31 puffs (mean difference -0.27 [CI, -0.49 to -0.04]) • Mean total asthma symptom score: -1.56 vs. –1.30 (mean difference -0.26 [CI, -0.42 to -0.10]) **Safety outcomes: (Omalizumab vs Placebo)** • Adverse events: 80.4% vs. 79.5% • Serious adverse events: 9.3% vs. 10.5%	**Exacerbation**: • Systemic corticosteroids for 3+ days • Increase oral steroid dose by 20mg prednisone

Severe Asthma: Omalizumab vs Placebo

Conclusion

Omalizumab provided additional benefit in patients with severe asthma that was uncontrolled with high-dose ICS-LABA

Omalizumab

ELIGIBILITY CRITERIA	DOSING
Positive skin prick test IgE and weight within dose range	Depends on weight and **pretreatment** IgE (Next slide)
PREDICTORS OF POSITIVE RESPONSE	**MONITORING** (PFTS, HYPERSENSITIVITY, AND INFECTION)
Blood eosinophils > 260/µL FeNO > 20 ppb Symptoms are driven by allergies Childhood onset asthma	Hypersensitivity reactions (45%) - **Black box warning** Infection: URI (2%), UTI (2%) Anti-antibody development: (<0.1%) Baseline serum total IgE

Omalizumab

Dosing

Dose depends on patient weight and **pretreatment** total IgE count

Dosing is **not** adjusted for changing IgE levels
Dosing **is** adjusted for changing body weight's
If therapy is interrupted for 1+ year then consider re-evaluating IgE count

Pretreatment serum IgE ≥30 to 100 units/mL
- 30 to 90 kg: 150 mg every 4 weeks
- >90 to 150 kg: 300 mg every 4 weeks

Pretreatment serum IgE >100 to 200 units/mL
- 30 to 90 kg: 300 mg every 4 weeks
- >90 to 150 kg: 225 mg every 2 weeks

Pretreatment serum IgE >200 to 300 units/mL
- 30 to 60 kg: 300 mg every 4 weeks
- >60 to 90 kg: 225 mg every 2 weeks
- >90 to 150 kg: 300 mg every 2 weeks

Pretreatment serum IgE >300 to 400 units/mL
- 30 to 70 kg: 225 mg every 2 weeks
- >70 to 90 kg: 300 mg every 2 weeks
- >90 kg: Use not recommended

Pretreatment serum IgE >400 to 500 units/mL
- 30 to 70 kg: 300 mg every 2 weeks
- >70 to 90 kg: 375 mg every 2 weeks
- >90 kg: Use not recommended

Pretreatment serum IgE >500 to 600 units/mL
- 30 to 60 kg: 300 mg every 2 weeks
- >60 to 70 kg: 375 mg every 2 weeks
- >70 kg: Use not recommended

Pretreatment serum IgE >600 to 700 units/mL
- 30 to 60 kg: 375 mg every 2 weeks
- >60 kg: Use not recommended

Biologic	Evidence	Eligibility (Exacerbation in the last year)	Positive Predictors	Dosing	Monitoring (PFTs, hypersensitivity, and infection)
Omalizumab	Omalizumab vs Placebo • Exacerbation rate: (0.66) vs (0.88) per patient • Δ AQLQ scores: (+1.15) vs. (+0.92) • Reduction in albuterol puffs: (-1.58) vs (-1.31) • Δ asthma symptom score: (-1.56) vs. (-1.30)	• Positive skin prick test • IgE and weight within dose range	• Blood eosinophils > 260/µL • FeNO > 20 ppb • Symptoms allergy driven • Childhood onset asthma	Depends on weight and **pretreatment** IgE	• **Hypersensitivity reactions (45%)** • Infection: URI (2%), UTI (2%) • Anti-antibody development: (<0.1%) • Baseline serum total IgE
Reslizumab					
Mepolizumab					
Benralizumab					
Dupilumab					
Tezepelumab-ekko					

Severe Asthma: Reslizumab vs Placebo

Objective	Evaluate the effect of reslizumab in patients with eosinophilic asthma uncontrolled with high-dose ICS
Methods	**Intervention**: reslizumab or placebo added to high dose ICS and at least one other agent (SABA, LABA, LTRA, or Cromolyn)
	Inclusion: • Age 18-75 • Confirmed airway reactivity or reversibility • High dose ICS + another agent • ACQ score > 1.5 **Exclusion**: • Taking systemic/oral steroids • Significant comorbid condition • Hypereosinophillic syndrome
Results	**Efficacy:** • Change in FEV(1): +7.3% vs -4% L [Mean difference 240mL (88 to 392mL)] • Reduction in eosinophils: 95.4% vs 38.7% (P = 0.007) • Asthma exacerbations: 8% vs 19% (P = 0.083) • Change in ACQ score for all patients: -0.7 vs -0.3 (P = 0.054) • Change in ACQ score for patients with nasal polyps: -1.0 vs -0.1 (P = 0.012) **Exacerbation**: • Systemic corticosteroids for 3+ days • A decrease of 20% or more in FEV_1 • Symptoms requiring emergency treatment • Hospital admission **Safety**: The most common adverse events with reslizumab were nasopharyngitis, fatigue, and pharyngolaryngeal pain

Castro M, Mathur S, Hargreave F, Boulet LP, Xie F, Young J, Wilkins HJ, Henkel T, Nair P; Res-5-0010 Study Group. Reslizumab for poorly controlled, eosinophilic asthma: a randomized, placebo-controlled study. Am J Respir Crit Care Med. 2011 Nov 15
Globe G, Wilkund I, Mattera M, Zhang H, Revicki DA. Evaluating minimal important differences and responder definitions for the asthma symptom diary in patients with moderate to severe asthma. J Patient Rep Outcomes. 2019 Apr 3.

Severe Asthma: Reslizumab vs Placebo

Conclusion

Add on reslizumab reduced sputum eosinophils, improved airway function, and provided better asthma control than add on placebo

Castro M, Mathur S, Hargreave F, Boulet LP, Xie F, Young J, Wilkins HJ, Henkel T, Nair P; Res-5-0010 Study Group. Reslizumab for poorly controlled, eosinophilic asthma: a randomized, placebo-controlled study. Am J Respir Crit Care Med. 2011 Nov 15

Reslizumab

ELIGIBILITY CRITERIA	DOSING
Blood eosinophils >150/µL	IV: 3 mg/kg once every 4 weeks

PREDICTORS OF POSITIVE RESPONSE	MONITORING (PFTS, HYPERSENSITIVITY, AND INFECTION)
Higher blood eosinophils More frequent exacerbations Adult-onset asthma Nasal polyposis	Hypersensitivity reactions: (0.3%) - **Black box warning** Infection: n/a Anti-antibody development: (5.4%) Baseline + periodic CBC with differential Increased creatine phosphokinase (20%)

Biologic	Evidence	Eligibility (Exacerbation in the last year)	Positive Predictors	Dosing	Monitoring (PFTs, hypersensitivity, and infection)
Omalizumab	**Omalizumab vs Placebo** • Exacerbation rate: 25% reduction • Δ AQLQ scores: (+1.15) vs. (+0.92) • Δ in albuterol puffs: (-1.58) vs (-1.31) • Δ asthma symptom score: (-1.56) vs. (-1.30)	• Positive skin prick test • IgE and weight within dose range	• Blood eosinophils > 260/µL • FeNO > 20 ppb • Symptoms allergy driven • Childhood onset asthma	Depends on weight and **pretreatment** IgE	• **Hypersensitivity reactions (45%)** • Infection: URI (2%), UTI (2%) • Anti-antibody development: (<0.1%) • Baseline serum total IgE
Reslizumab	**Reslizumab vs Placebo** • Asthma exacerbations: (8%) vs (19%) • Δ FEV1: (+7.3%) vs (-4%) • Reduction in eosinophils: (95.4%) vs (38.7%) • Δ ACQ - All patients: (-0.7) vs (-0.3) • Δ ACQ - Nasal polyps: (-1.0) vs (-0.1)	• Blood eosinophils >150/µL	• Higher blood eosinophils • More frequent exacerbations • Adult-onset asthma • Nasal polyposis	IV: 3 mg/kg once every 4 weeks	• **Hypersensitivity reactions: (0.3%)** • Infection: n/a • Anti-antibody development: (5.4%) • Baseline + periodic CBC with differential • Increased creatine phosphokinase (20%)
Mepolizumab					
Benralizumab					
Dupilumab					
Tezepelumab-ekko					

Severe Asthma: Mepolizumab vs Omalizumab

Objective	Assess if patients uncontrolled with omalizumab improve when switched to mepolizumab
Methods	**Intervention:** Patients continued omalizumab or switched to Mepolizumab 100 mg SQ every 4 weeks for 32 weeks
	Inclusion: • At least 2 asthma exacerbations in the past year • On high-dose ICS + another controller + omalizumab for ≥4 months • Eosinophil counts ≥150 at baseline or ≥300 in the past year • Asthma Control Questionnaire (ACQ)-5 score ≥1.5
Results	**Efficacy** • Change in ACQ-5 scores: 3.20 → 1.75 (-1.45 points, ≥0.5 points: 77%) • Change in SGRQ scores: 56.7 → 37.8 (-19.0 points, ≥4 points: 79%) • Annual rate of exacerbations: 63% reduction (1.18 vs 3.26 events/year) **Safety:** safety and immunogenicity profiles were consistent with previous trials

Exacerbation:
- Symptoms requiring ER visit
- Symptoms requiring hospitalization

Chapman KR, Albers FC, Chipps B, Muñoz X, Devouassoux G, Bergna M, Galkin D, Azmi J, Mouneimne D, Price RG, Liu MC. The clinical benefit of mepolizumab replacing omalizumab in uncontrolled severe eosinophilic asthma. Allergy. 2019 Sep
St. George's Respiratory Questionnaire (SGRQ). (n.d.)

Severe Asthma: Mepolizumab vs Omalizumab

Conclusion

Switching from omalizumab to mepolizumab resulted in significant improvements in asthma control, health status, and exacerbation rates

Chapman KR, Albers FC, Chipps B, Muñoz X, Devouassoux G, Bergna M, Galkin D, Azmi J, Mouneimne D, Price RG, Liu MC. The clinical benefit of mepolizumab replacing omalizumab in uncontrolled severe eosinophilic asthma. Allergy. 2019 Sep

Mepolizumab

ELIGIBILITY CRITERIA	DOSING
Blood eosinophils >150/µL	SUBQ: 100 mg once every 4 weeks

PREDICTORS OF POSITIVE RESPONSE	MONITORING (PFTS, HYPERSENSITIVITY, AND INFECTION)
Higher blood eosinophils More frequent exacerbations Adult-onset asthma Nasal polyposis	Hypersensitivity reactions: (0.3%) Hypersensitivity (15%) Infection UTI (3%), Influenza (5%) Anti-antibody development: (6%) Headache (19%)

Biologic	Evidence	Eligibility (Exacerbation in the last year)	Positive Predictors	Dosing	Monitoring (PFTs, hypersensitivity, and infection)
Omalizumab	**Omalizumab vs Placebo** • Exacerbation rate: 25% reduction • Δ AQLQ scores: (+1.15) vs. (+0.92) • Δ in albuterol puffs: (-1.58) vs (-1.31) • Δ asthma symptom score: (-1.56) vs. (-1.30)	• Positive skin prick test • IgE and weight within dose range	• Blood eosinophils > 260/µL • FeNO > 20 ppb • Symptoms allergy driven • Childhood onset asthma	Depends on weight and **pretreatment** IgE	• **Hypersensitivity reactions (45%)** • Infection: URI (2%), UTI (2%) • Anti-antibody development: (<0.1%) • Baseline serum total IgE
Reslizumab	**Reslizumab vs Placebo** • Asthma exacerbations: (8%) vs (19%) • Δ FEV1: (+7.3%) vs (-4%) • Reduction in eosinophils: (95.4%) vs (38.7%) • Δ ACQ - All patients: (-0.7) vs (-0.3) • Δ ACQ - Nasal polyps: (-1.0) vs (-0.1)	• Blood eosinophils >150/µL	• Higher blood eosinophils • More frequent exacerbations • Adult-onset asthma • Nasal polyposis	IV: 3 mg/kg once every 4 weeks	• **Hypersensitivity reactions: (0.3%)** • Infection: n/a • Anti-antibody development: (5.4%) • Baseline + periodic CBC with differential • Increased creatine phosphokinase (20%)
Mepolizumab	**Mepolizumab vs Omalizumab** • Rate of exacerbations: 63% reduction • Δ ACQ-5 scores:-1.45 points • Δ SGRQ scores: 19.0 points			SUBQ: 100 mg once every 4 weeks	• Hypersensitivity (15%) • Infection UTI (3%), Influenza (5%) • Anti-antibody development: (6%) • Headache (19%)
Benralizumab					
Dupilumab					
Tezepeluma b-ekko					

Severe Asthma: Benralizumab vs Placebo

Objective	Assess the safety and efficacy of benralizumab for patients with severe, uncontrolled asthma with eosinophilia
Methods	**Intervention**: Add on Benralizumab to ICS-LABA (Other controllers: tiotropium, LTRAs, chromone, theophylline, and OCS) • Benralizumab 30 mg every 4 weeks (Q4W) • Benralizumab 30mg every 8 weeks (Q8W)
	Inclusion: • Aged 12-75 years • Asthma for at least 1 year • At least 2 exacerbations on high-dosage ICS-LABA **Exclusion:** • anaphylaxis with any biologic drug • Lung disease other than asthma • Helminthic parasitic infection within 24 weeks before enrolment
Results	**Annual asthma exacerbation rate: (Benralizumab vs Placebo)** • Q4W dosing: rate ratio 0.55 (P<0.0001) • Q8W dosing: rate ratio 0.49 (P<0.0001) **Prebronchodilator FEV_1: (Benralizumab vs Placebo)** • Q4W dosing: 16.1% increase (+0.106 L) • Q8W dosing: 21.5% increase (+0.159 L) **Asthma symptoms (ACQ-6): (Benralizumab vs Placebo)** • Q4W dosing: mean difference –0.08 *Not statistically significant* • Q8W dosing: mean difference –0.25 • **Safety: (Benralizumab vs Placebo)** • Worsening asthma: 13% vs 19% • Nasopharyngitis: 12% vs 12%

Exacerbation:
- Use of oral corticosteroids
- Increase in stable oral corticosteroid dose for 3+ days
- injectable dose of corticosteroids
- ED or urgent care visit
- Hospital admission

Worsening asthma: any new or increased symptoms or signs

Bleecker ER, FitzGerald et al; SIROCCO study investigators. Efficacy and safety of benralizumab for patients with severe asthma uncontrolled with high-dosage inhaled corticosteroids and long-acting β2-agonists (SIROCCO): a randomised, multicentre, placebo-controlled phase 3 trial. Lancet. 2016 Oct 29

Benralizumab vs Placebo

Conclusion

Add on benralizumab is effective and safe for patients with severe asthma and elevated eosinophils that are uncontrolled with high-dose ICS-LABA

Bleecker ER, FitzGerald et al; SIROCCO study investigators. Efficacy and safety of benralizumab for patients with severe asthma uncontrolled with high-dosage inhaled corticosteroids and long-acting β2-agonists (SIROCCO): a randomised, multicentre, placebo-controlled phase 3 trial. Lancet. 2016 Oct 29

Benralizumab

ELIGIBILITY CRITERIA	DOSING
Blood eosinophils >150/µL	SUBQ: 30 mg every 4 weeks x3 doses, then every 8 weeks

PREDICTORS OF POSITIVE RESPONSE	MONITORING (PFTS, HYPERSENSITIVITY, AND INFECTION)
Higher blood eosinophils More frequent exacerbations Adult-onset asthma Nasal polyposis	Hypersensitivity reactions: (0.3%) Hypersensitivity: not listed Infection: Pharyngitis (5%) Anti-antibody development: (13%) Headache (8%)

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Biologic	Evidence	Eligibility (Exacerbation in the last year)	Positive Predictors	Dosing	Monitoring (PFTs, hypersensitivity, and infection)
Omalizumab	**Omalizumab vs Placebo** • Exacerbation rate: 25% reduction • Δ AQLQ scores: (+1.15) vs. (+0.92) • Δ in albuterol puffs: (-1.58) vs (-1.31) • Δ asthma symptom score: (-1.56) vs. (-1.30)	• Positive skin prick test • IgE and weight within dose range	• Blood eosinophils > 260/µL • FeNO > 20 ppb • Symptoms allergy driven • Childhood onset asthma	Depends on weight and **pretreatment** IgE	• **Hypersensitivity reactions (45%)** • Infection: URI (2%), UTI (2%) • Anti-antibody development: (<0.1%) • Baseline serum total IgE
Reslizumab	**Reslizumab vs Placebo** • Asthma exacerbations: (8%) vs (19%) • Δ FEV1: (+7.3%) vs (-4%) • Reduction in eosinophils: (95.4%) vs (38.7%) • Δ ACQ - All patients: (-0.7) vs (-0.3) • Δ ACQ - Nasal polyps: (-1.0) vs (-0.1)	• Blood eosinophils >150/µL	• Higher blood eosinophils • More frequent exacerbations • Adult-onset asthma • Nasal polyposis	IV: 3 mg/kg once every 4 weeks	• **Hypersensitivity reactions: (0.3%)** • Infection: n/a • Anti-antibody development: (5.4%) • Baseline + periodic CBC with differential • Increased creatine phosphokinase (20%)
Mepolizumab	**Mepolizumab vs Omalizumab** • Rate of exacerbations: 63% reduction • Δ ACQ-5 scores:-1.45 points • Δ SGRQ scores: 19.0 points			SUBQ: 100 mg once every 4 weeks	• Hypersensitivity (15%) • Infection UTI (3%), Influenza (5%) • Anti-antibody development: (6%) • Headache (19%)
Benralizumab	**Benralizumab vs Placebo** **Exacerbation rate** • Q4W Dosing: rate ratio 0.55 • Q8W Dosing: rate ratio 0.49 **Prebronchodilator FEV1** • Q4W dosing: +16.1) • Q8W dosing +21.5%			SUBQ: 30 mgQ4W x3 doses, then Q8W	• Hypersensitivity: not listed • Infection: Pharyngitis (5%) • Anti-antibody development: (13%) • Headache (8%)
Dupilumab					
Tezepeluma b-ekko					

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Severe Asthma: Dupilumab vs Placebo

Objective	Determine dupilumab's effectiveness in reducing oral glucocorticoids in severe asthma while maintaining asthma control
Methods	**Intervention**: • Dupilumab or placebo was added to background controller regimens • Glucocorticoid doses were weaned from week 4 to week 20 and then maintained at a stable dose for 4 weeks • Minimum dose without having an increase of 0.5 in the ACQ-5 score, a severe exacerbation, or an increase in OCS dose **Inclusion:** • Aged 12–75 years • Weighed at least 40 kg • Medium or high-dosage ICS-LABA for at least 1 year • At least 2 exacerbations requiring oral steroids or increase in ICS-LABA **Exclusion:** • Any other pulmonary or significant comorbid conditions • History of anaphylaxis to any biologic • Helminthic parasitic infection within 24 weeks before enrolment • Upper or Lower respiratory infection within 30 days of study
Results	**Efficacy: (Dupilumab vs placebo)** • Change in the oral steroid dose: -70.1% vs -41.9% (P<0.001) • Reduction of oral steroid dose of at least 50 percent: 80% vs 50% (P<0.001) • Reduction of dose to less than 5mg per day: 69% vs 33% (P<0.001) • Complete discontinuation of oral steroids: 48% vs 25% (P = 0.002) • Severe exacerbation rate per year: 0.649 vs 1.597 [59% lower than placebo (95% CI, 37% - 74%)] • Change in pre-bronchodilator FEV1: +18% vs +0.6% [mean difference 220mL (95% CI, 90 to 340 mL)] **Exacerbation**: • Hospitalization or ED visit • Oral steroid for 3+ days at ≥ 2x the previous dose **Safety (Dupilumab vs placebo)** • Injection-site reactions: 9% vs 4% • Transient blood eosinophilia: 14% vs 1%

Rabe KF et al Efficacy and Safety of Dupilumab in Glucocorticoid-Dependent Severe Asthma. N Engl J Med. 2018 Jun 28

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Severe Asthma: Dupilumab vs Placebo

Conclusion

Dupilumab treatment reduced oral glucocorticoid use, decreased severe exacerbations and increased FEV1.
Transient eosinophilia was observed in 1 in 7 dupilumab-treated patients

Why the Transient Eosinophilia?

- Hypothesis:
  - Dupilumab blocks eosinophils from migrating into tissue
  - Dupilumab does **NOT** block eosinophil production or release from bone marrow
  - A transient increase in circulating eosinophil counts results
  - Glucocorticoids suppress circulating eosinophils

Rabe KF et al Efficacy and Safety of Dupilumab in Glucocorticoid-Dependent Severe Asthma. N Engl J Med. 2018 Jun 28

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Dupilumab

ELIGIBILITY CRITERIA	DOSING
Any 1 of the following • Blood eosinophils 150 - 1500/µL • FeNO ≥ 25ppb • Taking maintenance OCS	SUBQ: 600 mg once, then 300 mg every other week
PREDICTORS OF POSITIVE RESPONSE	**MONITORING** (PFTS, HYPERSENSITIVITY, AND INFECTION)
Higher eosinophils Higher FeNO	Hypersensitivity (38%) Infection: URI (18%) Anti-antibody development: (6%) Arthralgia (3%) Ocular adverse effects (10%)

Biologic	Evidence	Eligibility (Exacerbation in the last year)	Positive Predictors	Dosing	Monitoring (PFTs, hypersensitivity, and infection)
Omalizumab	**Omalizumab vs Placebo** • Exacerbation rate: 25% reduction • Δ AQLQ scores: (+1.15) vs. (+0.92) • Δ in albuterol puffs: (-1.58) vs (-1.31) • Δ asthma symptom score: (-1.56) vs. (-1.30)	• Positive skin prick test • IgE and weight within dose range	• Blood eosinophils > 260/µL • FeNO > 20 ppb • Symptoms allergy driven • Childhood onset asthma	Depends on weight and **pretreatment** IgE	• **Hypersensitivity reactions (45%)** • Infection: URI (2%), UTI (2%) • Anti-antibody development: (<0.1%) • Baseline serum total IgE
Reslizumab	**Reslizumab vs Placebo** • Asthma exacerbations: (8%) vs (19%) • Δ FEV1: (+7.3%) vs (-4%) • Reduction in eosinophils: (95.4%) vs (38.7%) • Δ ACQ - All patients: (-0.7) vs (-0.3) • Δ ACQ - Nasal polyps: (-1.0) vs (-0.1)	• Blood eosinophils >150/µL	• Higher blood eosinophils • More frequent exacerbations • Adult-onset asthma • Nasal polyposis	IV: 3 mg/kg once every 4 weeks	• **Hypersensitivity reactions: (0.3%)** • Infection: n/a • Anti-antibody development: (5.4%) • Baseline + periodic CBC with differential • Increased creatine phosphokinase (20%)
Mepolizumab	**Mepolizumab vs Omalizumab** • Rate of exacerbations: 63% reduction • Δ ACQ-5 scores:-1.45 points • Δ SGRQ scores: 19.0 points			SUBQ: 100 mg once every 4 weeks	• Hypersensitivity (15%) • Infection:UTI (3%), Influenza (5%) • Anti-antibody development: (6%) • Headache (19%)
Benralizumab	**Benralizumab vs Placebo** **Exacerbation rate** • Q4W Dosing: rate ratio 0.55 • Q8W Dosing: rate ratio 0.49 **Prebronchodilator FEV1** • Q4W dosing: +16.1) • Q8W dosing +21.5%			SUBQ: 30 mgQ4W x3 doses, then Q8W	• Hypersensitivity: not listed • Infection: Pharyngitis (5%) • Anti-antibody development: (13%) • Headache (8%)
Dupilumab	**Dupilumab vs placebo** • Severe exacerbation rate: 59% reduction • Δ OCS dose: (-70.1%) vs (-41.9%) • Δ OCS dose of at least 50%: (80%) vs (50%) • OCS dose less than 5mg/day: (69%) vs (33%) • Complete discontinuation of OCS: (48%) vs (25%)	Any 1 of the following: • Blood eosinophils 150 - 1500/µL • FeNO ≥ 25ppb • Taking maintenance OCS	• Higher eosinophils • Higher FeNO	SUBQ: 600 mg x1, then 300 mg QOW	• Hypersensitivity (38%) • Infection: URI (18%) • Anti-antibody development: (6%) • Arthralgia (3%) • Ocular adverse effects (10%)
Tezepelumab-ekko					

Severe Asthma: Tezepelumab-ekko vs Placebo

Objective	Determine the efficacy and safety of tezepelumab in patients with severe, uncontrolled asthma.
Methods	**Intervention:** Add on tezepelumab 210mg or placebo SQ every 4 weeks for 52 weeks (added to ICS and additional controller medications)
	Inclusion: • Ages 12 to 80 • Medium or high-dose ICS + another controller for 12 months • FEV_1 < 80% of the predicted normal value • FEV_1 reversibility in the past year • At least two asthma exacerbations in the past 12 months **Exclusion:** • Any other pulmonary or significant comorbid conditions • History of cancer • Helminthic parasitic infection within 6 months before enrolment • Upper or Lower respiratory infection within 2 weeks of study • History of chronic alcohol or drug abuse
Results	**Efficacy: (Tezepelumab vs placebo)** • Rate of exacerbations per year: 56% reduction (0.93 vs 2.10, P<0.001) • Rate in patients with blood eosinophils < 300: 1.02 vs 1.73 (P<0.001) • Change in pre-bronchodilator FEV1: +33% vs +6.8% [Mean difference 230mL, (P<0.001)] • ACQ-6: -1.55 vs. -1.22 (P<0.001) • AQLQ: 1.49 vs. 1.15 (P<0.001) • ASD: -0.71 vs. -0.59 (P = 0.002) Exacerbation: • Hospitalization • ED visit that resulted in the use of systemic glucocorticoids for ≥3 consecutive days • Any use of systemic glucocorticoids for ≥3 consecutive days **Safety**: The frequencies and types of adverse events did not differ meaningfully between the two groups

Menzies-Gow A, Corren J, Bourdin A, Chupp G, Israel E, Wechsler ME, Brightling CE, Griffiths JM, Hellqvist Å, Bowen K, Kaur P, Almqvist G, Ponnarambil S, Colice G. Tezepelumab in Adults and Adolescents with Severe, Uncontrolled Asthma. N Engl J Med. 2021 May 13

Severe Asthma: Tezepelumab-ekko vs Placebo

Conclusion

Tezepelumab reduced exacerbations, improved lung function, improved asthma control, and improved health-related quality of life as compared to placebo.

Menzies-Gow A, Corren J, Bourdin A, Chupp G, Israel E, Wechsler ME, Brightling CE, Griffiths JM, Hellqvist Å, Bowen K, Kaur P, Almqvist G, Ponnarambil S, Colice G. Tezepelumab in Adults and Adolescents with Severe, Uncontrolled Asthma. N Engl J Med. 2021 May 13

Tezepelumab-ekko

ELIGIBILITY CRITERIA	DOSING
Exacerbation in the past year	SUBQ: 210 mg once every 4 weeks
PREDICTORS OF POSITIVE RESPONSE	**MONITORING** (PFTS, HYPERSENSITIVITY, AND INFECTION)
Higer eosinophils Higher FeNO	Hypersensitivity: not specified Infection: Pharyngitis (4%) Anti-antibody development: (5%)

Tezepelumab approved for self-administration with a new pre-filled pen

Published: 02/02/2023

Biologic	Evidence	Eligibility (Exacerbation in the last year)	Positive Predictors	Dosing	Monitoring (PFTs, hypersensitivity, and infection)
Omalizumab	**Omalizumab vs Placebo** • Exacerbation rate: 25% reduction • Δ AQLQ scores: (+1.15) vs. (+0.92) • Δ in albuterol puffs: (-1.58) vs (-1.31) • Δ asthma symptom score: (-1.56) vs. (-1.30)	• Positive skin prick test • IgE and weight within dose range	• Blood eosinophils > 260/µL • FeNO > 20 ppb • Symptoms allergy driven • Childhood onset asthma	Depends on weight and **pretreatment** IgE	• **Hypersensitivity reactions (45%)** • Infection: URI (2%), UTI (2%) • Anti-antibody development: (<0.1%) • Baseline serum total IgE
Reslizumab	**Reslizumab vs Placebo** • Asthma exacerbations: (8%) vs (19%) • Δ FEV1: (+7.3%) vs (-4%) • Reduction in eosinophils: (95.4%) vs (38.7%) • Δ ACQ - All patients: (-0.7) vs (-0.3) • Δ ACQ - Nasal polyps: (-1.0) vs (-0.1)	• Blood eosinophils >150/µL	• Higher blood eosinophils • More frequent exacerbations • Adult-onset asthma • Nasal polyposis	IV: 3 mg/kg once every 4 weeks	• **Hypersensitivity reactions: (0.3%)** • Infection: n/a • Anti-antibody development: (5.4%) • Baseline + periodic CBC with differential • Increased creatine phosphokinase (20%)
Mepolizumab	**Mepolizumab vs Omalizumab** • Rate of exacerbations: 63% reduction • Δ ACQ-5 scores:-1.45 points • Δ SGRQ scores: 19.0 points			SUBQ: 100 mg once every 4 weeks	• Hypersensitivity (15%) • Infection UTI (3%), Influenza (5%) • Anti-antibody development: (6%) • Headache (19%)
Benralizumab	**Benralizumab vs Placebo** **Exacerbation rate** • Q4W Dosing: rate ratio 0.55 • Q8W Dosing: rate ratio 0.49 **Prebronchodilator FEV1** • Q4W dosing: +16.1) • Q8W dosing +21.5%			SUBQ: 30 mgQ4W x3 doses, then Q8W	• Hypersensitivity: not listed • Infection: Pharyngitis (5%) • Anti-antibody development: (13%) • Headache (8%)
Dupilumab	**Dupilumab vs placebo** • Severe exacerbation rate: 59% reduction • Δ OCS dose: (-70.1%) vs (-41.9%) • Δ OCS dose of at least 50%: (80%) vs (50%) • OCS dose less than 5mg/day: (69%) vs (33%) • Complete discontinuation of OCS: (48%) vs (25%)	Any 1 of the following: • Blood eosinophils 150 - 1500/µL • FeNO ≥ 25ppb • Taking maintenance OCS	• Higher eosinophils • Higher FeNO	SUBQ: 600 mg x1, then 300 mg QOW	• Hypersensitivity (38%) • Infection: URI (18%) • Anti-antibody development: (6%) • Arthralgia (3%) • Ocular adverse effects (10%)
Tezepelumab-ekko	**Tezepelumab-ekko vs Placebo** • Rate of exacerbations: 56% reduction • Δ FEV1: +33% vs +6.8% • Δ ACQ-6: -1.55 vs. -1.22 (P<0.001) • Δ AQLQ: 1.49 vs. 1.15 (P<0.001) • Δ ASD: -0.71 vs. -0.59 (P = 0.002)	• Exacerbation in the past year	• Higer eosinophils • Higher FeNO	SUBQ: 210 mg once every 4 weeks.	• Hypersensitivity: not specified • Infection: Pharyngitis (4%) • Anti-antibody development: (5%)

Severe Asthma: Biologics Drug-Drug Interactions

Biologic	Interaction
Omalizumab	Loxapine -Risk X: Avoid combination
Reslizumab	No Risk X interactions
Mepolizumab	No Risk X interactions
Benralizumab	No Risk X interactions
Dupilumab	Vaccines (Live) - Risk X: Avoid combination
Tezepelumab	Vaccines (Live) - Risk X: Avoid combination

- All biologics interact with Efgartigimod Alfa (Myasthenia gravis immunosuppressive therapy)
- All agents are contraindicated if there is any history of hypersensitivity to agent or excipients

Severe Asthma: Biologics - Pharmacokinetics & Pharmacodynamics

Biologic	Absorption	Distribution	Metabolism	Elimination
Omalizumab	62%	78 mL/kg	Reticuloendothelial system and hepatic	T1/2 24 days
Reslizumab	--	5L	Proteolytic degradation	T1/2: 24 days
Mepolizumab	80%	3.6 L	Proteolytic degradation	T1/2: 16-22 days
Benralizumab	59%	2.5-3.1 L	Proteolytic degradation	T1/2: 15.5 days
Dupilumab	61% to 64%	~4.8 ± 1.3 L	Has not been characterized	Median time to undetectable: 9 - 11 weeks
Tezepelumab	77%	2.2-3.9 L	Proteolytic degradation	T1/2: 26 days

Severe Asthma: Biologics – Trial Duration

- Currently, there are no defined criteria for "good response"
  - Monitor the following:
    - Exacerbations
    - Symptom control - Asthma Control Test / Asthma Control Questionnaire (ACQ-5)
    - Lung function
    - Adverse events
    - Oral corticosteroid dose

Severe Asthma: Biologics – Trial Duration

- Initial Trial Duration: at least 4 months, then assess response
  - Good Response: re-evaluate every 3-6 months
    - Patient on OCS: Decrease OCS, asses for adrenal insufficiency, then discontinue OCS
    - Patient on High dose ICS: Decrease ICS for at least 3-6 months,
    - Biologic: re-evaluate necessity for biologic *No studies yet*
  - Unclear response: extend trial for another 6-10 months
  - No response: consider switching to another add-on therapy
    - Review basics
    - Stop Biologic
    - Consider chest CT
    - Re-assess phenotype
    - Consider OCS
    - Do not stop ICS

Severe Asthma: Biologics

Biologic	Preparation	Package AWP	Dosing Frequency	Administration location
Omalizumab	150 mg/mL	$1,465.38 per mL	Minimum: 150 mg every 4 weeks Maximum: 375 mg every 2 weeks	Clinic
Reslizumab	100 mg/10 mL	$123.48 per mL	3 mg/kg once every 4 weeks	Clinic
Mepolizumab	100 mg/mL	$3,990.41 per mL	100 mg once every 4 weeks	Clinic or Home
Benralizumab	30mg/mL	$6,421.06 per mL	30 mg every 4 weeks ***then*** 30 once every 8 weeks	Clinic or Home
Dupilumab	300mg / 2mL	$1,015.45 per mL	600 mg once ***then*** 300 mg every other week	Clinic
Tezepelumab	210 mg / 1.91mL	$2,282.51 per mL	210 mg once every 4 weeks.	Clinic or Home

Overcoming Cost - (Active hyperlinks)

	Estimated Annual Cost	Patient Assistance	Considerations
Omalizumab	$19,049.94 - $95,249.70	Omalizumab Copay Program	• $15,000 per year | $1,500 per year for administration • Cannot be in Genentech patient foundation
		Independent Copay assistance foundation	• Must call for referral (800) 704-6610
		Genentech Patient Foundation	• Must have income under $150,000
Reslizumab	$48,157.20	TEVA support solutions	• $10,000 per year • Does NOT cover physician visits/blood work • Must submit an explanation of benefits from insurance plan that details patients cost
Mepolizumab	$25,875.33	TEVA Cares Foundation	• n/a
		Mepolizumab Copay Program	• $15000 for 12 months | $100 per administration
Benralizumab	$51,368.48	Benralizumab Savings Program	• $13,000 per year | $100 per administration • Patients eligible for 365 days
		Denied Patient Savings Program	• Requires PA denial and PA appeal denial
Dupilumab	$54,834.30	Dupilumab copay Card	• $13,000 maximum benefit • Patients may be able to get reimbursed
		MyWay Patient Assistance Program	• Eligibility determined by the "*MyWay*" team
Tezepelumab	$56,674.72	Tezepelumab-ekko copay card	• Must call for max savings | $100 per month for administrations
		Tezepelumab-ekko "Fast Start" Program	• Patients may stay in the program for 2 years • Up to 12 doses at no cost while insurance coverage is secured • Must submit PA or PA appeal within 60 days

Role of the Pharmacist

- Assess technique, adherence, and environmental exposures before escalating therapy
- Place emphasis on treating asthma phenotype
- Emphasize the importance of positive predictors when selecting a biologic agent
- Attempt to de-escalate therapy appropriate time intervals (Biologic, OCS, high-dose ICS-LABA)
- Ensure adequate dosing for biologics
- Be aware of which biologics require administration in a clinicians' office

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Role of Technicians

- Identify insurance requirements that must be satisfied for patient assistance programs
- Identify candidates for financial support (Insured vs Uninsured vs Government Insurance)
- Understand when patients should receive their refills and order the appropriate quantity of medication

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