

# An Update on Asthma Medications

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A decorative graphic consisting of several horizontal lines of varying lengths and colors (teal, light blue, white) extending from the right side of the slide towards the center.

# Outline

- Review the newest medications used for the treatment of asthma including:  
    Bronchodilators, Corticosteroids and  
    Cytokine Modulators.
- Review the most current anti-allergy medications on the market.
- Demonstrate the use of new inhalers.

# New bronchodilators

## ProAir RespiClick (albuterol sulfate)

- First and only FDA-approved, multi-dose, breath-actuated, dry-powder rescue inhaler for patient 12 years and older. Indicated for the treatment or prevention of bronchospasm with reversible obstructive airway disease and for the prevention of exercise-induced bronchospasm.

NDC 59310-540-20  
Rx Only



# ProAir<sup>®</sup> RespiClick

(albuterol sulfate)  
Inhalation Powder

**With Dose Counter**

**FOR ORAL INHALATION ONLY  
SEE WARNINGS INSTRUCTIONS  
FOR USE AND CONTENTS**

Refer to enclosed Patient Leaflet and  
Instructions for Use for detailed  
information on product use and handling.



# ProAir RespiClick

- 2 inhalations every 4–6 hours; in some patients: 1 inhalation every 4 hours may suffice. Exercise-induced bronchospasm: 2 inhalations 15–30 minutes before exercise.
- Supplied as an inhaler (with dose counter)—200 inhalations.

# ProAir RespiClick Pearls

- Throw away ProAir RespiClick 13 months after removing it from the foil pouch for the first time, when the dose counter displays '0,' or after the expiration date on the package, whichever comes first.
- Do not open the cap unless you are taking a dose. Opening and closing the cap without inhaling a dose will waste the medicine and may damage your inhaler.

# Adverse events

- Adverse events that occurred at an incidence rate of at least 1% and greater than placebo included:
  - back pain (2% vs 1%), pain (2% vs <1%), gastroenteritis viral (1% vs <1%), sinus headache (1% vs <1%), and urinary tract infection (1% vs <1%).



# Contraindications

- Contraindicated in patients with hypersensitivity to albuterol or patients with a *severe hypersensitivity to milk proteins*. Rare cases of hypersensitivity reactions, including urticaria, angioedema, and rash have been reported after the use of albuterol sulfate. There have been reports of anaphylactic reactions in patients using inhalation therapies containing *lactose*.

# Breo Ellipta (fluticasone furoate & vilanterol)

- BREO® ELLIPTA® for the once-daily treatment of asthma in patients aged 18 years and older. Two strengths, 100/25mcg and 200/25mcg, have been approved in the US for use in asthma, administered once-daily using the Ellipta dry powder inhaler.



**gsk** GlaxoSmithKline

NDC 0173-0859-10  
Rx Only

# BREO™ ELLIPTA™

(fluticasone furoate and vilanterol  
inhalation powder)

**FOR ORAL INHALATION ONLY**

Each blister on one strip contains 100 mcg of fluticasone furoate and lactose monohydrate. Each blister on the other strip contains 25 mcg of vilanterol, magnesium stearate, and lactose monohydrate.

**100 mcg/25 mcg**

Federal Law requires the dispensing of BREO ELLIPTA with the Medication Guide inside the carton.

1 ELLIPTA™ Inhaler containing 2 Foil Strips of 30 Blisters each

**gsk**  
GlaxoSmithKline  
NDC 0173-0859-10 Rx Only

**BREO™ ELLIPTA™**  
(fluticasone furoate and vilanterol  
inhalation powder) **100 mcg/25 mcg**  
**FOR ORAL INHALATION ONLY**

Tray opened:

Discard  
(6 weeks):

29

1 ELLIPTA™  
Inhaler  
containing  
2 Foil Strips of  
30 Blisters  
each

# Breo Ellipta pearls

- If you open and close the cover without inhaling the medicine, you will lose the dose. The lost dose will be securely held inside the inhaler, but it will no longer be available to be inhaled.
- It is not possible to accidentally take a double dose or an extra dose in one inhalation.
- The inhaler contains 30 doses (14 doses if you have a sample or institutional pack).
- The “discard” date is 6 weeks from the date you open the tray.

# Adverse reactions

- Most common adverse reactions (incidence greater than or equal to 2%) are:
  - nasopharyngitis, oral candidiasis, headache, influenza, upper respiratory tract infection, bronchitis, sinusitis, oropharyngeal pain, dysphonia, and cough.

# Spiriva (tiotropium) Respimat

- Long-acting, 24-hour, anticholinergic bronchodilator approved for asthma in September 2015.
- Used for maintenance treatment of asthma in patients 12 years and older.
- Two inhalations (2.5 mcg) once daily (maximum: 2 inhalations per 24 hours). Note: Maximum benefits may take up to 4 to 8 weeks of dosing.
- Not indicated for the relief of acute bronchospasm.

# Spiriva® Respimat®

2.5 microgram,  
Solution for Inhalation

Tiotropium



ยาควบคุมพิเศษ  
ใช้เฉพาะสถานพยาบาล

Single pack:  
1 Respimat® Inhaler and  
1 cartridge contains 4.0 ml providing 60 puffs



Boehringer  
Ingelheim



# Spiriva (tiotropium) Respimat

- If not used for more than 3 days, actuate the inhaler once to prepare the inhaler for use (Canadian labeling indicates that this process is required if the inhaler has not been used for more than 7 days). If not used for more than 21 days, actuate the inhaler until an aerosol cloud is visible and then repeat the process three more times to prepare the inhaler for use.



# Spiriva (tiotropium) Respimat

- Common adverse drug reactions ( $\geq 1\%$  of patients) associated with tiotropium therapy include: dry mouth and/or throat irritation. Rarely ( $< 0.1\%$  of patients) treatment is associated with: urinary retention, constipation, acute angle closure glaucoma, palpitations (notably supraventricular tachycardia and atrial fibrillation) and/or allergy (rash, angioedema, anaphylaxis).

# Arnuity Ellipta (fluticasone furoate)

- Arnuity Ellipta is a prescription inhaled corticosteroid medicine taken as 1 inhalation, once daily, for the control and prevention of asthma in adults and children aged 12 years and older.
- No prior treatment with inhaled corticosteroids: Initial: 100 mcg once daily; maximum: 200 mcg once daily.
- Prior treatment with inhaled corticosteroids: Initial: 100 to 200 mcg once daily; maximum: 200 mcg once daily.



# Adverse reactions (>10%)

- Central nervous system: Fatigue ( $\leq 16\%$ ), malaise ( $\leq 16\%$ ), headache (2% to 14%).
- Gastrointestinal: Oral candidiasis ( $\leq 31\%$ ).
- Neuromuscular & skeletal: Arthralgia ( $\leq 17\%$ ), arthritis ( $\leq 17\%$ ), musculoskeletal pain (2% to 12%).
- Respiratory: Sinus infection ( $\leq 33\%$ ), sinusitis ( $\leq 33\%$ ), upper respiratory tract infection (2% to 31%), throat irritation (<1% to 22%), nasal congestion ( $\geq 3\%$  to 16%), nasopharyngitis (8% to 13%), rhinitis (<1% to 13%), bronchitis ( $\leq 12\%$ ).

# Risk of LABA's

- Increased risk of overall death if monotherapy
- Evidence supports LABA + ICS in a single inhaler device for patient with mod/severe asthma

# Biologics

- Biopharmaceutical approaches have identified new therapies that target key cells and mediators that drive inflammatory responses in the asthmatic lung.
- Inflammation of asthma is caused by T helper cells which release cytokines such as IL4, IL5, IL13 contributing to eosinophil inflammation and IgE production.

## Biologics (con't)

- Issues remain with regard to the cost of biologics, determination of the most effective biomarkers to select responsive patients and whether treatment with biologics should be confined to specialist asthma centers.
- One other important consideration is that the placebo group in trials of biologics in asthma often exhibit a marked improvement in symptoms, which may reduce the likelihood of significant findings being observed for the test compound.

# IgE Xolair (omalizumab)

- 1st molecule targeted by anti-IgE monoclonal antibodies for treatment of asthma.
- Binds IgE in the circulation and prevents it from activating mast cells and basophils.
- Anti IgE therapy is recommended as an add-on to optimized standard therapy in asthmatics 12 years and older who need continuous or frequent treatment with oral corticosteroids.
- Elevated serum IgE 30-700 IU/ml. Positive allergy test.



# Nucala (mepolizumab)

- Effective in reducing blood and sputum eosinophils. **Approved in June 2015.** Given once every four weeks.
- The results of studies demonstrate that mepolizumab is efficacious in patients with specific phenotypes of severe asthma characterized by persistent, glucocorticosteroid-resistant eosinophilia; re-emphasizing the importance of the pathogenic role of the IL-5–eosinophil axis in selected subgroups of patients with severe asthma, with special regard to the recurrence of asthma exacerbations.

# Other biologics under investigation

- Reslizumab – IL-5
- Benralizumab – effector cells whose functions are driven by IL-5
- Lebrikizumab – IL-13
- Tralokinumab – IL-13
- Dupilumab – IL-4, IL-13

# Anti-Allergy Medications

- Timothy grass extract : Grastek
  - Used for grass pollen-induced allergic rhinitis confirmed by positive allergy testing
  - Dose one tablet sublingual daily. Leave under tongue for at least 1 minute.
  - Start 12 weeks before grass season
  - Ages 5-65
  - Do not use in severe or uncontrolled asthma.

# Anti-Allergy Medications (con't)

- Grass pollen extract: Oralair
  - Used for treatment of grass pollen-induced allergic rhinitis confirmed by positive allergy testing
  - 5 grass species included
  - Dose one sublingual daily
  - Ages 10-65
  - Do not use in uncontrolled asthma

# Anti-Allergy Medications (con't)

- Short Ragweed Pollen Extract: Ragwitek
  - Indicated as immunotherapy for the treatment of short ragweed pollen-induced allergic rhinitis confirmed by positive allergy testing
  - Dose one tablet sublingual daily
  - Start 12 weeks prior to season
  - Ages 18-65
  - Do not use in severe or uncontrolled asthma

# Phenotypes of asthma

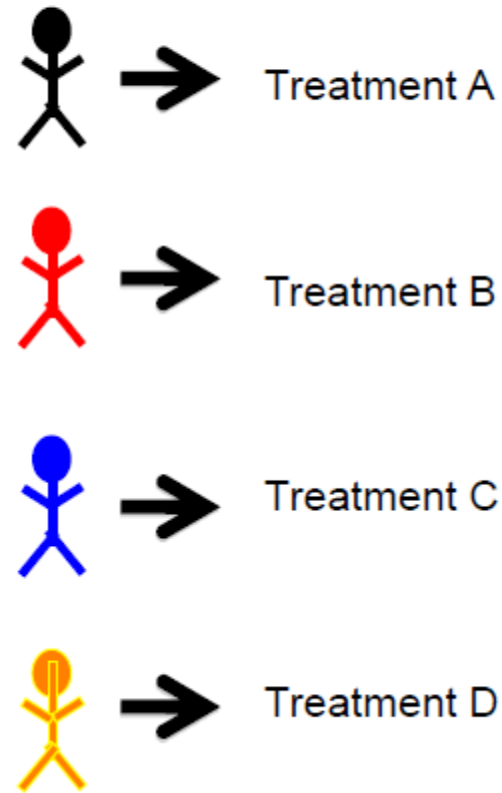
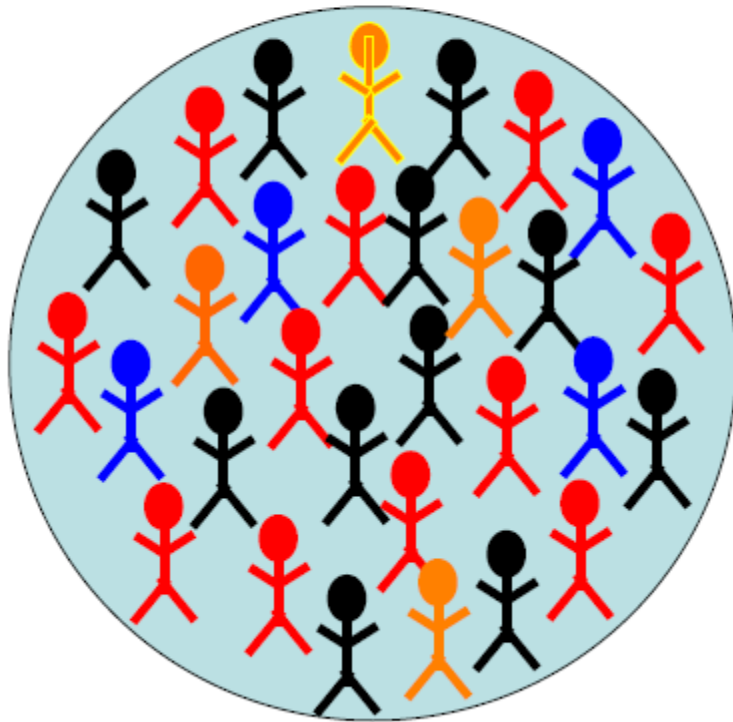
- Asthma is a heterogeneous disease. Identification of specific subphenotypes of asthma may further our understanding of pathophysiology and treatment response, leading to the better targeting of both existing and novel antiasthma therapies.

# Phenotypes of asthma

- Phenotype: Any observable characteristic of a disease (morphology, biochemical or physiological properties) without any implication for mechanism.
- Endotype: A subtype of a condition, defined by a distinct functional or pathobiological mechanism.

# Asthma Treatment- Where do we need to go?

## Personalized Medicine based on endotype





# Other/Experimental therapies

- Nebulized heparin
  - In vitro studies have shown that heparin decreases inflammation, smooth muscle proliferation, eosinophil recruitment, and fibrosis.
  - The effect of nebulized heparin on airway inflammation and hyperresponsiveness has been evaluated in patients with asthma and allergic rhinitis.

# Other/Experimental therapies

- Immune modulatory therapy
  - Numerous agents with antiinflammatory properties have been studied in an effort to eliminate or decrease the inflammation that underlies chronic asthma. These agents include methotrexate, gold, cyclosporine, colchicine, hydroxychloroquine, intravenous immunoglobulin (IVIG), dapsone, macrolide antibiotics, etanercept, and infliximab.

# Other/Experimental therapies

- TNF- $\alpha$  inhibitors – overall, studies do NOT support a beneficial effect for anti-TNF-alpha agents in the treatment of asthma.
- GATA3-specific DNzyme is a transcription factor that is essential for Th2 lymphocyte differentiation and activation

# Other/Experimental therapies

- Novel glucocorticoid receptor agonist - the novel glucocorticoid receptor agonist AZD5423 is a nonsteroidal compound that binds to the glucocorticoid receptor in a different manner from traditional glucocorticoids. It appears to suppress production of proinflammatory proteins (like traditional glucocorticoids), but with reduced adverse effects in animal models.

# Other/Experimental therapies

- Thymic stromal lymphopoietin (TSLP) is an epithelial-cell–derived cytokine that may be important in initiating allergic inflammation and, thus, play a role in allergic asthma.
- Antifungal therapy - it is hypothesized that inhalational exposure to airborne fungi may lead to low level airway colonization, sufficient to cause an ongoing allergic reaction, although clinical trials have not found sustained improvement in asthma control with antifungal therapy.

# Other/Experimental therapies

- Herbal medicines — Chinese herbs
- Homeopathic agents — The US Food and Drug Administration (FDA) has issued a warning to consumers not to rely on homeopathic products for asthma.

The image features a central graphic consisting of several concentric circles. The outermost circle is a dark red, and the inner circles transition through lighter shades of red to a dark blue center. Overlaid on this graphic is the text "That's all Folks!" written in a white, elegant cursive font. The text is positioned diagonally across the center of the circles.

*That's all Folks!*