Dupixent (dupilumab)

NEW INDICATION REVIEW

MPR

Introduction

- **Brand name:** Dupixent
- **Generic name:** Dupilumab
- **Pharmacological class:** Interleukin-4 receptor alpha antagonist
- **Strength and Formulation:** 200mg/1.14mL, 300mg/2mL; soln for SC inj; preservative-free
- **Manufacturer:** Sanofi and Regeneron
- **How supplied:** Single-dose prefilled syringes—2 (with needle shield)
- **Legal Classification:** Rx

Dupixent


NDC 0024-5918-01
Rx Only
DUPIXENT®
(dupilumab)
Injection
200 mg/1.14 mL (175 mg/mL)
For Subcutaneous Use Only
2 Single-dose Pre-filled Syringes with Needle Shield
200 mg/1.14 mL
SANOFI GENZYME
REGENERON


NDC 0024-5914-01
Rx Only
DUPIXENT®
(dupilumab)
Injection
300 mg/2 mL (150 mg/mL)
For Subcutaneous Injection Only
2 Single-dose Pre-filled Syringes with Needle Shield
300 mg/2 mL
SANOFI GENZYME
REGENERON

New Indication

- Add-on maintenance treatment in patients with moderate-to-severe asthma aged ≥12yrs with an eosinophilic phenotype or with oral corticosteroid dependent asthma
- Limitations of use: Not for relief of acute bronchospasm or status asthmaticus

Other Indication

- Also indicated for:
  - Moderate-to-severe atopic dermatitis in adults who are not adequately controlled with topical prescription therapies or when they are not advisable

Dosage & Administration

- **Moderate-to-severe asthma**
  - Give by SC inj into thigh, abdomen (except around navel), or upper arm; rotate inj sites
  - Initially 400mg (given as two 200mg inj at different sites) followed by 200mg every other week; **or**
  - Initially 600mg (given as two 300mg inj at different sites) followed by 300mg every other week

Dosage & Administration

- **Moderate-to-severe asthma**
  - **For those with oral corticosteroids-dependent asthma or with co-morbid moderate-to-severe atopic dermatitis for which Dupixent is indicated:** initially 600mg followed by 300mg every other week

  - *See full labeling for additional dosing information*

Considerations for Special Populations

- **Pediatric:** <12yrs: not established
- **Pregnancy:** Available data have not identified a drug-associated risk; human IgG antibodies are known to cross the placental barrier
- **Nursing mothers:** Consider mother's need and potential adverse effects on child
- **Elderly:** No differences in safety or efficacy observed

Warnings/Precautions

- **Discontinue** if significant hypersensitivity reaction occurs; treat appropriately
- Advise patients to report new onset or worsening **eye symptoms**
- Atopic dermatitis patients with co-morbid asthma
- Pre-existing helminth infections; treat prior to Dupixent initiation
- Do not inject into tender, damaged, bruised or scarred skin

Interactions

- **Avoid** concomitant live vaccines
- Concomitant CYP450 substrates with narrow therapeutic index (eg, warfarin, cyclosporine); monitor and consider dose adjustment

Adverse Reactions

- Injection site reactions
- Conjunctivitis
- Blepharitis
- Oral herpes
- Keratitis
- Eye pruritus
- Other herpes simplex virus infection
- Dry eye
- Hypersensitivity
- Also in asthma studies:
  - Oropharyngeal pain
  - Eosinophilia

Mechanism of Action

- Dupilumab is a human monoclonal IgG4 antibody that inhibits interleukin-4 (IL-4) and interleukin-13 (IL-13) signaling by specifically binding to the IL-4Rα subunit shared by the IL-4 and IL-13 receptor complexes

- Blocking IL-4Rα with dupilumab inhibits IL-4 and IL-13 cytokine-induced inflammatory responses, including the release of proinflammatory cytokines, chemokines, nitric oxide, and IgE; however, the mechanism of dupilumab action in asthma has not been definitively established

Clinical Studies

- The asthma development program included 3 randomized, double-blind, placebo-controlled, parallel-group, multicenter trials (**AS Trials 1, 2, and 3**) of 24 to 52 weeks in duration which enrolled patients aged 12 years and older (N=2888)

Clinical Studies

- **AS Trial 2** was a 52-week study which included 1902 patients with moderate-to-severe asthma on a medium or high-dose inhaled corticosteroid and a minimum of 1 and up to 2 additional controller medications
- Patients were randomized to 200mg or 300mg Dupixent Q2W (or matching placebo for either 200mg or 300mg Q2W) following an initial dose of 400mg, 600mg or placebo respectively
- **Primary endpoints**: annualized rate of severe exacerbation events and change from baseline in pre-bronchodilator FEV_1

Clinical Studies

- In the overall population, the **rate of severe exacerbations** was 0.46 and 0.52 for Dupixent 200mg Q2W and 300mg Q2W, respectively, compared to matched placebo rates of 0.87 and 0.97

- The **rate ratio of severe exacerbations** compared to placebo was 0.52 (95% CI: 0.41, 0.66) and 0.54 (95% CI: 0.43, 0.68) for Dupixent 200mg Q2W and 300mg Q2W, respectively

Clinical Studies

- Greater reductions in severe exacerbations were observed in patients with higher baseline blood eosinophil levels (≥150 cells/μL)
- In patients with baseline blood eosinophils of ≥300 cells/μL, treatment with dupilumab reduced severe exacerbations by 67% compared with placebo

Clinical Studies

- In the overall population, the **FEV_1 LS mean change from baseline** was 0.32L (21%) and 0.34L (23%) for Dupixent 200mg Q2W and 300mg Q2W, respectively, compared to matched placebo means of 0.18L (12%) and 0.21L (14%)
- The **mean treatment difference** vs placebo was 0.14L (95% CI: 0.08, 0.19) and 0.13L (95% CI: 0.08, 0.18) for Dupixent 200mg Q2W and 300mg Q2W, respectively
- Subgroup analysis demonstrated greater improvement in patients with higher baseline blood eosinophils

Clinical Studies

- **AS Trial 3** evaluated the effect of Dupixent on reducing the use of maintenance oral corticosteroids
- The baseline mean oral corticosteroid dose was 12mg in the placebo group and 11mg in the Dupixent group
- The **primary endpoint** was the percent reduction from baseline of the final oral corticosteroid dose at Week 24 while maintaining asthma control

Clinical Studies

- Compared with placebo, patients receiving Dupixent achieved greater reductions in daily maintenance oral corticosteroid dose, while maintaining asthma control
- The mean percent reduction in daily OCS dose from baseline was 70% (median 100%) in the Dupixent arm (95% CI: 60%, 80%) compared with 42% (median 50%) in the placebo group (95% CI: 33%, 51%)

Clinical Studies

- **Reductions of 50% or higher** in the OCS dose were observed in 80% of patients receiving Dupixent vs 53% in those receiving placebo
- The proportion of patients with a mean final dose <5mg at Week 24 was 72% for Dupixent and 37% for placebo (odds ratio 4.48 95% CI: 2.39, 8.39)
- 52% of patients in the Dupixent arm had a **100% reduction** in their OCS dose vs 29% in the placebo group
- For more clinical data, see full labeling

Product Monograph

- For more information view the product monograph available at:

  http://www.empr.com/dupixent/drug/34658/