CLINICAL UPDATE

Brand Name	Dupixent®
Generic Name	dupilumab
Drug Manufacturer	Regeneron Pharmaceuticals, Inc.

Clinical Update

TYPE OF CLINICAL UPDATE

Updated Indication and Strength

FDA APPROVAL DATE

October 20,2021

LAUNCH DATE

N/A

REVIEW DESIGNATION

N/A

TYPE OF REVIEW

Biologic License Application (BLA): 761055

DISPENSING RESTRICTIONS

Specialty Pharmacy Required

Overview

INDICATION(S) FOR USE

Dupixent® is an interleukin-4 receptor alpha antagonist indicated:

- For the treatment of patients aged 6 years and older with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. Dupixent® can be used with or without topical corticosteroids.
- As an add-on maintenance treatment of patients aged 6 years and older with moderate-to-severe asthma characterized by an eosinophilic phenotype or with oral corticosteroid dependent asthma.
- As an add-on maintenance treatment in adult patients with inadequately controlled chronic rhinosinusitis with nasal polyposis (CRSwNP).

MECHANISMS 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. Dupilumab inhibits IL-4 signaling via the Type I receptor and both IL-4 and IL-13 signaling through the Type II receptor.

Inflammation driven by IL-4 and IL-13 is an important component in the pathogenesis of asthma, atopic dermatitis, and CRSwNP. Multiple cell types that express IL-4Rα (e.g., mast cells, eosinophils, macrophages, lymphocytes, epithelial cells, goblet cells) and inflammatory mediators (e.g., histamine, eicosanoids, leukotrienes, cytokines,

chemokines) are involved in inflammation. 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. The mechanism of dupilumab action in asthma has not been definitively established.

DOSAGE FORM(S) AND STRENGTH(S)

- Injection: 300 mg/2 mL solution in a single-dose pre-filled pen.
- Injection: 300 mg/2 mL solution in a single-dose pre-filled syringe with needle shield.
- Injection: 200 mg/1.14 mL solution in a single-dose pre-filled pen.
- Injection: 200 mg/1.14 mL solution in a single-dose pre-filled syringe with needle shield.
- Injection: 100 mg/0.67 mL solution in a single-dose pre-filled syringe with needle shield.

DOSE & ADMINISTRATION

Administer by subcutaneous injection. The Dupixent® pre-filled pen is only for use in adults and adolescents aged 12 years and older.

Atopic Dermatitis

Dosage in Adults:

The recommended dosage is an initial dose of 600 mg (two 300 mg injections in different injection sites), followed by 300 mg given every other week (Q2W).

Dosage in Pediatric Patients (6 to 17 Years of Age):

Body Weight	**Initial Loading Dose**	**Subsequent Doses** [a]
15 to less than 30 kg	600 mg (two 300 mg injections)	300 mg Q4W
30 to less than 60 kg	400 mg (two 200 mg injections)	200 mg Q2W
60 kg or more	600 mg (two 300 mg injections)	300 mg Q2W

Q2W – every other week; Q4W – every 4 weeks

Asthma

Dosage in Adults and Adolescents (12 Years and Older):

Initial Loading Dose	**Subsequent Dose**
400 mg (two 200 mg injections)	200 mg every 2 weeks (Q2W)
or	
600 mg (two 300 mg injections)	300 mg every 2 weeks (Q2W)
Dosage for patients with oral corticosteroid-dependent asthma or with comorbid moderate-to-severe atopic dermatitis or adults with co-morbid chronic rhinosinusitis with nasal polyposis	
600 mg (two 300 mg injections)	300 mg every 2 weeks (Q2W)

Dosage in Pediatric Patients (6 to 11 Years of Age):

Body Weight	Initial Dose and Subsequent Doses
15 to less than 30 kg	100 mg every other week (Q2W) or 300 mg every four weeks (Q4W)
≥30 kg	200 mg every other week (Q2W)

For pediatric patients (6 to 11 years old) with asthma and co-morbid moderate-to severe atopic dermatitis, follow the recommended dosage as per Table 1 which includes an initial loading dose.

Chronic Rhinosinusitis with Nasal Polyposis
The recommended dosage of Dupixent® for adult patients is 300 mg given every other week.

EFFICACY

Atopic Dermatitis

The safety and effectiveness of Dupixent® have been established in pediatric patients 6 years of age and older with moderate-to-severe atopic dermatitis. Use of Dupixent® in this age group is supported by Trial 6 which included 251 adolescents ages 12 to 17 years old with moderate-to-severe atopic dermatitis and Trial 8 which included 367 children ages 6 to 11 years old with severe atopic dermatitis. The safety and effectiveness were generally consistent between pediatric and adult patients.

Efficacy Results of Dupixent® in Trial 6 at Week 16 (FAS)a:

	DUPIXENT[d] 200 mg (<60 kg) or 300 mg (≥60 kg) Q2W N=82[a]	Placebo N=85[a]
IGA 0 or 1[b,c]	24%	2%
EASI-75[c]	42%	8%
EASI-90[c]	23%	2%
Peak Pruritus NRS (≥4-point improvement)[c]	37%	5%

[a] Full Analysis Set (FAS) includes all subjects randomized.
[b] Responder was defined as a subject with an IGA 0 or 1 ("clear" or "almost clear") and a reduction of ≥2 points on a 0-4 IGA scale.
[c] Subjects who received rescue treatment or with missing data were considered as non-responders (59% and 21% in the placebo and DUPIXENT arms, respectively).
[d] At Week 0, subjects received 400 mg (baseline weight <60 kg) or 600 mg (baseline weight ≥60 kg) of DUPIXENT.

Efficacy Results of Dupixent® with Concomitant TCS in Trial 8 at Week 16 (FAS)a:

	DUPIXENT 300 mg Q4W[d] + TCS (N=61)	Placebo + TCS (N=61)	DUPIXENT 200 mg Q2W[e] + TCS (N=59)	Placebo + TCS (N=62)
	<30 kg	<30 kg	≥30 kg	≥30 kg
IGA 0 or 1[b,c]	30%	13%	39%	10%
EASI-75[c]	75%	28%	75%	26%
EASI-90[c]	46%	7%	36%	8%
Peak Pruritus NRS (≥4-point improvement)[c]	54%	12%	61%	13%

[a] Full Analysis Set (FAS) includes all subjects randomized.
[b] Responder was defined as a subject with an IGA 0 or 1 ("clear" or "almost clear").
[c] Subjects who received rescue treatment or with missing data were considered as non-responders.
[d] At Day 1, subjects received 600 mg of DUPIXENT.

Asthma

The safety and effectiveness of Dupixent® for an add-on maintenance treatment in patients with moderate-to-severe asthma characterized by an eosinophilic phenotype or with oral corticosteroid dependent asthma have been established in pediatric patients 6 years of age and older. Use of Dupixent® for this indication is supported by evidence from adequate and wellcontrolled studies in adult and pediatric patients 6 years and older.

Efficacy Results of Dupixent® in AS Trial 4:

Treatment	**EOS ≥300 cells/mcL[a]**		
Annualized Severe Exacerbations Rate over 52 Weeks			
	N	**Rate (95% CI)**	**Rate Ratio (95% CI)**
DUPIXENT 100 mg Q2W(<30 kg)/ 200 mg Q2W (≥30 kg)	175	0.24 (0.16, 0.35)	0.35 (0.22, 0.56)
Placebo	84	0.67 (0.47, 0.95)	

Mean Change from Baseline in Percent Predicted FEV_1 at Week 12			
	N	**LS mean Δ from Baseline**	**LS mean difference vs. Placebo (95% CI)**
DUPIXENT 100 mg Q2W (<30 kg)/ 200 mg Q2W (≥30 kg)	168	10.15	5.32 (1.76, 8.88)
Placebo	80	4.83	

[a] This reflects the prespecified primary analysis population for AS Trial 4 in the United States.