FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Atopic Dermatitis

DUPIXENT is indicated for the treatment of adult and pediatric patients aged 6 months and older with moderate-to-severe atopic dermatitis (AD) 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.

1.2 Asthma

DUPIXENT is indicated as an add-on maintenance treatment of adult and pediatric patients aged 6 years and older with moderate-to-severe asthma characterized by an eosinophilic phenotype or with oral corticosteroid dependent asthma *[see Clinical Studies (14)]*.

Limitations of Use

DUPIXENT is not indicated for the relief of acute bronchospasm or status asthmaticus.

1.3 Chronic Rhinosinusitis with Nasal Polyposis

DUPIXENT is indicated as an add-on maintenance treatment in adult patients with inadequately controlled chronic rhinosinusitis with nasal polyposis (CRSwNP).

1.4 Eosinophilic Esophagitis

DUPIXENT is indicated for the treatment of adult and pediatric patients aged 12 years and older, weighing at least 40 kg, with eosinophilic esophagitis (EoE).

1.5 Prurigo Nodularis

DUPIXENT is indicated for the treatment of adult patients with prurigo nodularis (PN).

2 DOSAGE AND ADMINISTRATION

2.1 Important Administration Instructions

DUPIXENT is administered by subcutaneous injection.

DUPIXENT is intended for use under the guidance of a healthcare provider. Provide proper training to patients and/or caregivers on the preparation and administration of DUPIXENT prior to use according to the "Instructions for Use".

Use of Pre-filled Pen or Pre-filled Syringe

The DUPIXENT pre-filled pen is for use in adult and pediatric patients aged 2 years and older.

The DUPIXENT pre-filled syringe is for use in adult and pediatric patients aged 6 months and older.

A caregiver or patient 12 years of age and older may inject DUPIXENT using the pre-filled syringe or pre-filled pen. In pediatric patients 12 to 17 years of age, administer DUPIXENT under the supervision of an adult. In pediatric patients 6 months to less than 12 years of age, administer DUPIXENT by a caregiver.

Administration Instructions

For AD, asthma, and PN patients taking an initial 600 mg dose, administer each of the two DUPIXENT 300 mg injections at different injection sites.

For AD and asthma patients taking an initial 400 mg dose, administer each of the two DUPIXENT 200 mg injections at different injection sites.

Administer subcutaneous injection into the thigh or abdomen, except for the 2 inches (5 cm) around the navel. The upper arm can also be used if a caregiver administers the injection.

Rotate the injection site with each injection. DO NOT inject DUPIXENT into skin that is tender, damaged, bruised, or scarred.

The DUPIXENT "Instructions for Use" contains more detailed instructions on the preparation and administration of DUPIXENT *[see Instructions for Use]*.

2.2 Vaccination Prior to Treatment

Consider completing all age-appropriate vaccinations as recommended by current immunization guidelines prior to initiating treatment with DUPIXENT *[see Warnings and Precautions (5.9)]*.

2.3 Recommended Dosage for Atopic Dermatitis

Dosage in Adults

The recommended dosage of DUPIXENT for adult patients is an initial dose of 600 mg (two 300 mg injections), followed by 300 mg given every other week (Q2W).

Dosage in Pediatric Patients 6 Months to 5 Years of Age

The recommended dosage of DUPIXENT for pediatric patients 6 months to 5 years of age is specified in Table 1.

Table 1: Dosage of DUPIXENT in Pediatric Patients 6 Months to 5 Years of Age with Atopic Dermatitis

Body Weight	Initial[a] and Subsequent Dosage
5 to less than 15 kg	200 mg (one 200 mg injection) every 4 weeks (Q4W)
15 to less than 30 kg	300 mg (one 300 mg injection) every 4 weeks (Q4W)

[a] For pediatric patients 6 months to 5 years of age with AD, no initial loading dose is recommended.

Dosage in Pediatric Patients 6 Years to 17 Years of Age

The recommended dosage of DUPIXENT for pediatric patients 6 years to 17 years of age is specified in Table 2.

Table 2: Dosage of DUPIXENT in Pediatric Patients 6 Years to 17 Years of Age with Atopic Dermatitis

Body Weight	Initial Loading Dose	Subsequent Dosage
15 to less than 30 kg	600 mg (two 300 mg injections)	300 mg every 4 weeks (Q4W)
30 to less than 60 kg	400 mg (two 200 mg injections)	200 mg every other week (Q2W)
60 kg or more	600 mg (two 300 mg injections)	300 mg every other week (Q2W)

Concomitant Topical Therapies

DUPIXENT can be used with or without topical corticosteroids. Topical calcineurin inhibitors may be used, but should be reserved for problem areas only, such as the face, neck, intertriginous and genital areas.

2.4 Recommended Dosage for Asthma

Dosage in Adult and Pediatric Patients 12 Years and Older

The recommended dosage of DUPIXENT for adult and pediatric patients 12 years of age and older is specified in Table 3.

Table 3: Dosage of DUPIXENT in Adult and Pediatric Patients 12 Years and Older with Asthma

Initial Loading Dose	Subsequent Dosage
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 co-morbid 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

The recommended dosage of DUPIXENT for pediatric patients 6 to 11 years of age is specified in Table 4.

Table 4: Dosage of DUPIXENT in Pediatric Patients 6 to 11 Years of Age with Asthma

Body Weight	Initial[a] and Subsequent Dosage
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)

[a] For pediatric patients 6 to 11 years of age with asthma, no initial loading dose is recommended.

For pediatric patients 6 to 11 years of age with asthma and co-morbid moderate-to-severe AD, follow the recommended dosage as per Table 2 which includes an initial loading dose *[see Dosage and Administration (2.3)]*.

2.5 Recommended Dosage for Chronic Rhinosinusitis with Nasal Polyposis

The recommended dosage of DUPIXENT for adult patients is 300 mg given every other week.

2.6 Recommended Dosage for Eosinophilic Esophagitis

The recommended dosage of DUPIXENT for adult and pediatric patients 12 years of age and older, weighing at least 40 kg, is 300 mg given every week (QW).

2.7 Recommended Dosage for Prurigo Nodularis

The recommended dosage of DUPIXENT for adult patients is an initial dose of 600 mg (two 300 mg injections) followed by 300 mg given every other week (Q2W).

2.8 Missed Doses

If a weekly dose is missed, administer the dose as soon as possible, and start a new weekly schedule from the date of the last administered dose.

If an every other week dose is missed, administer the injection within 7 days from the missed dose and then resume the patient's original schedule. If the missed dose is not administered within 7 days, wait until the next dose on the original schedule.

If an every 4 week dose is missed, administer the injection within 7 days from the missed dose and then resume the patient's original schedule. If the missed dose is not administered within 7 days, administer the dose, starting a new schedule based on this date.

2.9 Preparation for Use

Before injection, remove DUPIXENT from the refrigerator and allow DUPIXENT to reach room temperature (45 minutes for the 300 mg/2 mL pre-filled syringe or pre-filled pen, 30 minutes for the 200 mg/1.14 mL pre-filled syringe or pre-filled pen, and 100 mg/0.67 mL pre-filled syringe) without removing the needle cap. After removal from the refrigerator, DUPIXENT must be used within 14 days or discarded.

Inspect DUPIXENT visually for particulate matter and discoloration prior to administration. DUPIXENT is a clear to slightly opalescent, colorless to pale yellow solution. Do not use if the liquid contains visible particulate matter, is discolored or cloudy (other than clear to slightly opalescent, colorless to pale yellow). DUPIXENT does not contain preservatives; therefore, discard any unused product remaining in the pre-filled syringe or pre-filled pen.

3 DOSAGE FORMS AND STRENGTHS

DUPIXENT is a clear to slightly opalescent, colorless to pale yellow solution in a:

Single-dose pre-filled syringe with needle shield as:

- Injection: 300 mg/2 mL
- Injection: 200 mg/1.14 mL
- Injection: 100 mg/0.67 mL

Single-dose pre-filled pen as:

- Injection: 300 mg/2 mL
- Injection: 200 mg/1.14 mL

4 CONTRAINDICATIONS

DUPIXENT is contraindicated in patients who have known hypersensitivity to dupilumab or any excipients of DUPIXENT *[see Warnings and Precautions (5.1)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity

Hypersensitivity reactions, including anaphylaxis, serum sickness or serum sickness-like reactions, angioedema, generalized urticaria, rash, erythema nodosum, and erythema multiforme have been reported. If a clinically significant hypersensitivity reaction occurs, institute appropriate therapy and discontinue DUPIXENT *[see Adverse Reactions (6.1, 6.2, 6.3)]*.

5.2 Conjunctivitis and Keratitis

Conjunctivitis and keratitis adverse reactions have been reported in clinical trials.

Conjunctivitis and keratitis occurred more frequently in AD subjects who received DUPIXENT compared to those who received placebo. Conjunctivitis was the most frequently reported eye disorder. Most subjects with conjunctivitis or keratitis recovered or were recovering during the treatment period *[see Adverse Reactions (6.1)]*.

In subjects with CRSwNP, the frequency of conjunctivitis was 2% in the DUPIXENT group compared to 1% in the placebo group in the 24-week safety pool; these subjects recovered. There were no cases of keratitis reported in the CRSwNP development program *[see Adverse Reactions (6.1)]*.

Among subjects with asthma, the frequencies of conjunctivitis and keratitis were similar between DUPIXENT and placebo *[see Adverse Reactions (6.1)]*.

Among subjects with EoE, the frequency of conjunctivitis and keratitis was 0% and 0% in the DUPIXENT group and 2% and 0% in the placebo group, respectively *[see Adverse Reactions (6.1)]*.

In subjects with PN, the frequency of conjunctivitis was 4% in the DUPIXENT group compared to 1% in the placebo group; these subjects recovered or were recovering during the treatment period. There were no cases of keratitis reported in the PN development program *[see Adverse Reactions (6.1)]*.

Conjunctivitis and keratitis adverse events have also been reported with DUPIXENT in postmarketing settings, predominantly in AD patients. Some patients reported visual disturbances (e.g., blurred vision) associated with conjunctivitis or keratitis.

Advise patients to report new onset or worsening eye symptoms to their healthcare provider. Consider ophthalmological examination for patients who develop conjunctivitis that does not resolve following standard treatment or signs and symptoms suggestive of keratitis, as appropriate *[see Adverse Reactions (6.1)]*.

5.3 Eosinophilic Conditions

Patients being treated for asthma may present with serious systemic eosinophilia sometimes presenting with clinical features of eosinophilic pneumonia or vasculitis consistent with eosinophilic granulomatosis with polyangiitis, conditions which are often treated with systemic corticosteroid therapy. These events may be associated with the reduction of oral corticosteroid therapy. Healthcare providers should be alert to vasculitic rash, worsening pulmonary symptoms, cardiac complications, and/or neuropathy presenting in their patients with eosinophilia. Cases of eosinophilic pneumonia were reported in adult subjects who participated in the asthma development program and cases of vasculitis consistent with eosinophilic granulomatosis with polyangiitis have been reported with DUPIXENT in adult subjects who participated in the asthma development program as well as in adult subjects with co-morbid asthma in the CRSwNP development program. A causal association between DUPIXENT and these conditions has not been established.

5.4 Acute Asthma Symptoms or Deteriorating Disease

DUPIXENT should not be used to treat acute asthma symptoms or acute exacerbations. Do not use DUPIXENT to treat acute bronchospasm or status asthmaticus. Patients should seek medical advice if their asthma remains uncontrolled or worsens after initiation of treatment with DUPIXENT.

5.5 Risk Associated with Abrupt Reduction of Corticosteroid Dosage

Do not discontinue systemic, topical, or inhaled corticosteroids abruptly upon initiation of therapy with DUPIXENT. Reductions in corticosteroid dose, if appropriate, should be gradual and performed under the direct supervision of a healthcare provider. Reduction in corticosteroid dose may be associated with systemic withdrawal symptoms and/or unmask conditions previously suppressed by systemic corticosteroid therapy.

5.6 Patients with Co-morbid Asthma

Advise patients with co-morbid asthma not to adjust or stop their asthma treatments without consultation with their physicians.

5.7 Arthralgia

Arthralgia has been reported with the use of DUPIXENT with some patients reporting gait disturbances or decreased mobility associated with joint symptoms; some cases resulted in hospitalization *[see Adverse Reactions (6.1)]*. In postmarketing reports, onset of arthralgia was

variable, ranging from days to months after the first dose of DUPIXENT. Some patients' symptoms resolved while continuing treatment with DUPIXENT and other patients recovered or were recovering following discontinuation of DUPIXENT.

Advise patients to report new onset or worsening joint symptoms to their healthcare provider. If symptoms persist or worsen, consider rheumatological evaluation and/or discontinuation of DUPIXENT.

5.8 Parasitic (Helminth) Infections

Patients with known helminth infections were excluded from participation in clinical studies. It is unknown if DUPIXENT will influence the immune response against helminth infections.

Treat patients with pre-existing helminth infections before initiating therapy with DUPIXENT. If patients become infected while receiving treatment with DUPIXENT and do not respond to anti-helminth treatment, discontinue treatment with DUPIXENT until the infection resolves. Adverse reactions of helminth infections (5 cases of enterobiasis and 1 case of ascariasis) were reported in pediatric patients 6 to 11 years old who participated in the pediatric asthma development program *[see Adverse Reactions (6.1)]*.

5.9 Vaccinations

Consider completing all age-appropriate vaccinations as recommended by current immunization guidelines prior to initiating treatment with DUPIXENT. Avoid use of live vaccines in patients treated with DUPIXENT. It is unknown if administration of live vaccines during DUPIXENT treatment will impact the safety or effectiveness of these vaccines. Limited data are available regarding coadministration of DUPIXENT with non-live vaccines *[see Clinical Pharmacology (12.2)]*.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Hypersensitivity *[see Warnings and Precautions (5.1)]*
- Conjunctivitis and Keratitis *[see Warnings and Precautions (5.2)]*
- Arthralgia *[see Warnings and Precautions (5.7)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Adults with Atopic Dermatitis

Three randomized, double-blind, placebo-controlled, multicenter trials (SOLO 1, SOLO 2, and CHRONOS) and one dose-ranging trial (AD-1021) evaluated the safety of DUPIXENT in subjects with moderate-to-severe AD. The safety population had a mean age of 38 years; 41% of subjects were female, 67% were White, 24% were Asian, and 6% were Black; in terms of co-morbid conditions, 48% of the subjects had asthma, 49% had allergic rhinitis, 37% had food

allergy, and 27% had allergic conjunctivitis. In these 4 trials, 1472 subjects were treated with subcutaneous injections of DUPIXENT, with or without concomitant topical corticosteroids (TCS).

A total of 739 subjects were treated with DUPIXENT for at least 1 year in the development program for moderate-to-severe AD.

SOLO 1, SOLO 2, and AD-1021 compared the safety of DUPIXENT monotherapy to placebo through Week 16. CHRONOS compared the safety of DUPIXENT + TCS to placebo + TCS through Week 52.

AD-1225 is a multicenter, open-label extension (OLE) study which assessed the long-term safety of repeat doses of DUPIXENT (through 148 weeks of treatment) in adults with moderate-to-severe AD who had previously participated in controlled studies of DUPIXENT or had been screened for SOLO 1 or SOLO 2. The safety data in AD-1225 reflect exposure to DUPIXENT in 2677 subjects, including 2254 exposed for at least 52 weeks, 1192 exposed for at least 100 weeks, and 357 exposed for at least 148 weeks. In AD-1225, 99.7% of subjects were exposed to DUPIXENT 300 mg weekly dosing (QW).

Weeks 0 to 16 (SOLO 1, SOLO 2, CHRONOS, and AD-1021)

In DUPIXENT monotherapy trials (SOLO 1, SOLO 2, and AD-1021) through Week 16, the proportion of subjects who discontinued treatment because of adverse events was 1.9% in both the DUPIXENT 300 mg Q2W and placebo groups. Table 5 summarizes the adverse reactions that occurred at a rate of at least 1% in the DUPIXENT 300 mg Q2W monotherapy groups, and in the DUPIXENT + TCS group, all at a higher rate than in their respective comparator groups during the first 16 weeks of treatment.

Table 5: Adverse Reactions Occurring in ≥1% of the DUPIXENT Monotherapy Group or the DUPIXENT + TCS Group in the Atopic Dermatitis Trials through Week 16

Adverse Reaction	DUPIXENT Monotherapy[a]		DUPIXENT + TCS[b]	
	DUPIXENT 300 mg Q2W[c] N=529 n (%)	Placebo N=517 n (%)	DUPIXENT 300 mg Q2W[c] + TCS N=110 n (%)	Placebo + TCS N=315 n (%)
Injection site reaction	51 (10)	28 (5)	11 (10)	18 (6)
Conjunctivitis[d]	51 (10)	12 (2)	10 (9)	15 (5)
Blepharitis	2 (<1)	1 (<1)	5 (5)	2 (1)
Oral herpes	20 (4)	8 (2)	3 (3)	5 (2)
Keratitis[e]	1 (<1)	0	4 (4)	0
Eye pruritus	3 (1)	1 (<1)	2 (2)	2 (1)
Other herpes simplex virus infection[f]	10 (2)	6 (1)	1 (1)	1 (<1)
Dry eye	1 (<1)	0	2 (2)	1 (<1)

[a] Pooled analysis of SOLO 1, SOLO 2, and AD-1021.
[b] Analysis of CHRONOS where subjects were on background TCS therapy.
[c] DUPIXENT 600 mg at Week 0, followed by 300 mg every two weeks.
[d] Conjunctivitis cluster includes conjunctivitis, allergic conjunctivitis, bacterial conjunctivitis, viral conjunctivitis, giant papillary conjunctivitis, eye irritation, and eye inflammation.