HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use DUPIXENT safely and effectively. See full prescribing information for DUPIXENT.

DUPIXENT® (dupilumab) injection, for subcutaneous use

Initial U.S. Approval: 2017

RECENT MAJOR CHANGES

INDICATIONS AND USAGE

DUPIXENT is an interleukin-4 receptor alpha antagonist indicated:

• for the treatment of patients aged 12 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. (1.1)

• as an add-on maintenance treatment in patients with moderate-to-severe asthma aged 12 years and older with an eosinophilic phenotype or with oral corticosteroid dependent asthma. (1.2)

• as an add-on maintenance treatment in adult patients with inadequately controlled chronic rhinosinusitis with nasal polyposis (CRSwNP). (1.3)

DOSE AND ADMINISTRATION

Administer by subcutaneous injection. (2)

Atopic Dermatitis

Adults

• The recommended dose is an initial dose of 600 mg (two 300 mg injections in different injection sites), followed by 300 mg given every other week. (2.1)

Adolescents

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>Initial Dose</th>
<th>Subsequent Doses (every other week)</th>
</tr>
</thead>
<tbody>
<tr>
<td>less than 60 kg</td>
<td>400 mg (two 200 mg injections)</td>
<td>200 mg</td>
</tr>
<tr>
<td>60 kg or more</td>
<td>600 mg (two 300 mg injections)</td>
<td>300 mg</td>
</tr>
</tbody>
</table>

Asthma

• The recommended dose of DUPIXENT for adults and adolescents (12 years of age and older) is:
  - an initial dose of 400 mg (two 200 mg injections) followed by 200 mg given every other week or
  - an initial dose of 600 mg (two 300 mg injections) followed by 300 mg given every other week
  - for patients requiring concomitant oral corticosteroids or with co-morbid moderate-to-severe atopic dermatitis for which DUPIXENT is indicated, start with an initial dose of 600 mg followed by 300 mg given every other week (2.2)

Chronic Rhinosinusitis with Nasal Polyposis

• The recommended dose of DUPIXENT for adult patients is 300 mg given every other week. (2.3)

DOSE FORMS AND STRENGTHS

- Injection: 300 mg/2 mL solution in a single-dose pre-filled syringe with needle shield (3)
- Injection: 200 mg/1.14 mL solution in a single-dose pre-filled syringe with needle shield (3)

CONTRAINDICATIONS

Known hypersensitivity to DUPIXENT or any of its excipients. (4)

WARNINGS AND PRECAUTIONS

- Hypersensitivity: Hypersensitivity reactions (urticaria, rash, erythema nodosum, anaphylaxis, and serum sickness) have occurred after administration of DUPIXENT. Discontinue DUPIXENT in the event of a hypersensitivity reaction. (5.1)

- Conjunctivitis and Keratitis: Patients should report new onset or worsening eye symptoms to their healthcare provider. (5.2)

- Eosinophilic Conditions: Be alert to vasculitic rash, worsening pulmonary symptoms, and/or neuropathy, especially upon reduction of oral corticosteroids. (5.3)

- Reduction of Corticosteroid Dosage: Do not discontinue systemic, topical, or inhaled corticosteroids abruptly upon initiation of therapy with DUPIXENT. Decrease steroids gradually, if appropriate. (5.5)

- Parasitic (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. (5.7)

ADVERSE REACTIONS

Atopic Dermatitis: Most common adverse reactions (incidence ≥1%) are injection site reactions, conjunctivitis, blepharitis, oral herpes, keratitis, eye pruritus, other herpes simplex virus infection, and dry eye. (6.1)

Asthma: Most common adverse reactions (incidence ≥1%) are injection site reactions, oropharyngeal pain, and eosinophilia. (6.1)

Chronic Rhinosinusitis with Nasal Polyposis: Most common adverse reactions (incidence ≥1%) are injection site reactions, eosinophilia, insomnia, toothache, gastritis, arthralgia, and conjunctivitis. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Regeneron at 1-844-387-4938 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

Live Vaccines: Avoid use of live vaccines with DUPIXENT. (7.1)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 06/2019

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2.2 Asthma

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2. DURATION OF ADMINISTRATION

DUPIXENT is administered by subcutaneous injection.

2.1 Atopic Dermatitis

Dosing in Adults

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

Dosing in Adolescents

The recommended dose of DUPIXENT for patients 12 to 17 years of age is specified in Table 1.

Table 1: Dose of DUPIXENT for Subcutaneous Administration in Adolescent Patients

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>Initial Dose</th>
<th>Subsequent Doses (every other week)</th>
</tr>
</thead>
<tbody>
<tr>
<td>less than 60 kg</td>
<td>400 mg (two 200 mg injections)</td>
<td>200 mg</td>
</tr>
<tr>
<td>60 kg or more</td>
<td>600 mg (two 300 mg injections)</td>
<td>300 mg</td>
</tr>
</tbody>
</table>

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.

2.2 Asthma

The recommended dose of DUPIXENT for adults and adolescents (12 years of age and older) is:

- an initial dose of 400 mg (two 200 mg injections) followed by 200 mg given every other week or
- an initial dose of 600 mg (two 300 mg injections) followed by 300 mg given every other week
- for patients with oral corticosteroid-dependent asthma, or with co-morbid moderate-to-severe atopic dermatitis for which DUPIXENT is indicated, start with an initial dose of 600 mg followed by 300 mg given every other week

2.3 Chronic Rhinosinusitis with Nasal Polyps

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

2.4 Important Administration Instructions

DUPIXENT is intended for use under the guidance of a healthcare provider. A patient may self-inject DUPIXENT after training in subcutaneous injection technique using the pre-filled syringe. Provide proper training to patients and/or caregivers on the preparation and administration of DUPIXENT prior to use according to the “Instructions for Use”.

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

For 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.

If a dose is missed, instruct the patient to 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, instruct the patient to wait until the next dose on the original schedule.

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

2.5 Preparation for Use of DUPIXENT Pre-filled Syringe with Needle Shield

Before injection, remove DUPIXENT pre-filled syringe from the refrigerator and allow DUPIXENT to reach room temperature (45 minutes for the 300 mg/2 mL pre-filled syringe and 30 minutes for the 200 mg/1.14 mL pre-filled syringe) without removing the needle cap.

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.

3. DOSAGE FORMS AND STRENGTHS

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

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

4. CONTRAINDICATIONS

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

5. WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity

Hypersensitivity reactions, including generalized urticaria, rash, erythema nodosum and serum sickness or serum sickness-like reactions, were reported in less than 1% of subjects who received DUPIXENT in clinical trials. Two subjects in the atopic dermatitis development program experienced serum sickness or serum sickness-like reactions that were associated with high titers of antibodies to dupilumab. One subject in the asthma development program experienced anaphylaxis [see Adverse Reactions (6.2)]. If a clinically significant hypersensitivity reaction occurs, institute appropriate therapy and discontinue DUPIXENT [see Adverse Reactions (6.1, 6.2)].

5.2 Conjunctivitis and Keratitis

Conjunctivitis and keratitis occurred more frequently in atopic dermatitis subjects who received DUPIXENT. Conjunctivitis was the most frequently reported eye disorder. Most subjects with conjunctivitis recovered or were recovering during the treatment period. Keratitis was reported in <1% of the DUPIXENT group (1 per 100 subject-years) and in 0% of the placebo group (0 per 100 subject-years) in the 16-week atopic dermatitis monotherapy trials. In the 52-week DUPIXENT + topical corticosteroids (TCS) atopic dermatitis trial, keratitis was reported in 4% of the DUPIXENT + TCS group (12 per 100 subject-years) and in 0% of the placebo + TCS group (0 per 100 subject-years). Most subjects with keratitis recovered or were recovering during the treatment period [see Adverse Reactions (6.1)].

Among asthma subjects, the frequencies of conjunctivitis and keratitis were similar between DUPIXENT and placebo [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)].

Advise patients to report new onset or worsening eye symptoms to their healthcare provider.

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 polyanlitis, conditions which are often treated with systemic corticosteroid therapy. These events may be associated with the reduction of oral corticosteroid therapy. Physicians 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 patients who participated in the asthma development program and cases of vasculitis consistent with eosinophilic granulomatosis with polyangiitis have been reported with DUPIXENT in adult patients who participated in the asthma development program as well as three patients 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 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 physician. Reduction in corticosteroid dose may be associated with systemic withdrawal symptoms and/or mask conditions previously suppressed by systemic corticosteroid therapy.

5.6 Patients with Co-morbid Asthma
Advise patients with atopic dermatitis or CRSwNP who have co-morbid asthma not to adjust or stop their treatments without consultation with their physicians.

5.7 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.

6 ADVERSE REACTIONS

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.

Adulthood with Atopic Dermatitis

Three randomized, double-blind, placebo-controlled, multicenter trials (Trials 1, 2, and 3) and one dose-ranging trial (Trial 4) evaluated the safety of DUPIXENT in subjects with moderate-to-severe atopic dermatitis. The safety population had a mean age of 38 years; 41% of subjects were female, and 26% 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 atopic dermatitis. Trials 1, 2, and 4 compared the safety of DUPIXENT monotherapy to placebo through Week 16. Trial 3 compared the safety of DUPIXENT + TCS to placebo + TCS through Week 52.

Weeks 0 to 16 (Trials 1 to 4):
In DUPIXENT monotherapy trials (Trials 1, 2, and 4) 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 2 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>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>DUPIXENT Monotherapy</th>
<th>DUPIXENT + TCS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Injection site reaction</strong></td>
<td>N=529 n (%)</td>
<td>N=517 n (%)</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>51 (10)</td>
<td>25 (5)</td>
</tr>
<tr>
<td>Blepharitis</td>
<td>2 (&lt;1)</td>
<td>1 (&lt;1)</td>
</tr>
<tr>
<td>Oral herpes</td>
<td>5 (2)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Keratitis</td>
<td>1 (1)</td>
<td>4 (4)</td>
</tr>
<tr>
<td>Eye pruritus</td>
<td>3 (1)</td>
<td>1 (&lt;1)</td>
</tr>
<tr>
<td>Other herpes simplex virus infection</td>
<td>10 (2)</td>
<td>6 (1)</td>
</tr>
<tr>
<td>Dry eye</td>
<td>1 (1)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

Table 2 summarizes the adverse reactions that occurred at a rate of at least 1% in the DUPIXENT + TCS Group in the Atopic Dermatitis Trials through Week 16.

Safety through Week 52 (Trial 3):

In the DUPIXENT with concomitant TCS trial (Trial 3) through Week 52, the proportion of subjects who discontinued treatment because of adverse events was 1.8% in DUPIXENT 300 mg Q2W + TCS group and 7.6% in the placebo + TCS group. Two subjects discontinued DUPIXENT because of adverse reactions: atopic dermatitis (1 subject) and exfoliative dermatitis (1 subject).

The safety profile of DUPIXENT + TCS through Week 52 was generally consistent with the safety profile observed at Week 16.

Adolescents with Atopic Dermatitis

The safety of DUPIXENT was assessed in a trial of 250 subjects 12 to 17 years of age with moderate-to-severe atopic dermatitis (Trial 6). The safety profile of DUPIXENT in these subjects through Week 16 was similar to the safety profile from studies in adults with atopic dermatitis.

The long-term safety of DUPIXENT was assessed in an open-label extension study in subjects 12 to 17 years of age with moderate-to-severe atopic dermatitis (Trial 7). The safety profile of DUPIXENT in subjects followed through Week 52 was similar to the safety profile observed at Week 16 in Trial 6. The long-term safety profile of DUPIXENT observed in adolescents was consistent with that seen in adults with atopic dermatitis.

A total of 2888 adult and adolescent subjects with moderate-to-severe asthma (AS) were evaluated in 3 randomized, placebo-controlled, multicenter trials of 24 to 52 weeks duration (AS Trials 1, 2, and 3). Of these, 2679 had a history of 1 or more severe exacerbations in the year prior to enrollment despite regular use of medium to high-dose inhaled corticosteroids plus an additional controller(s) (AS Trials 1 and 2). A total of 210 subjects with oral corticosteroid-dependent asthma receiving high-dose inhaled corticosteroids plus up to two additional controllers were enrolled (AS Trial 3). The safety population (AS Trials 1 and 2) was 12-87 years of age, of which 63% were female, and 82% were white. DUPIXENT 200 mg or 300 mg was administered subcutaneously Q2W, following an initial dose of 400 mg or 600 mg, respectively.

In AS Trials 1 and 2, the proportion of subjects who discontinued treatment due to adverse events was 4% of the placebo group, 3% of the DUPIXENT 200 mg Q2W group, and 6% of the DUPIXENT 300 mg Q2W group.

Table 3 summarizes the adverse reactions that occurred at a rate of at least 1% in subjects treated with DUPIXENT and at a higher rate than in their respective comparator groups in Asthma Trials 1 and 2.

Table 3: Adverse Reactions Occurring in ≥1% of the DUPIXENT Groups in Asthma Trials 1 and 2 and Greater than Placebo (6 Month Safety Pool)

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>DUPIXENT 200 mg Q2W</th>
<th>DUPIXENT 300 mg Q2W</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injection site reactions</td>
<td>111 (14%)</td>
<td>144 (18%)</td>
<td>50 (6%)</td>
</tr>
<tr>
<td>Oral pharyngeal pain</td>
<td>13 (2%)</td>
<td>19 (2%)</td>
<td>7 (1%)</td>
</tr>
<tr>
<td>Eosinophilia</td>
<td>17 (2%)</td>
<td>16 (2%)</td>
<td>2 (&lt;1%)</td>
</tr>
</tbody>
</table>

Injection site reactions were most common with the loading (initial) dose.

The safety profile of DUPIXENT through Week 52 was generally consistent with the safety profile observed at Week 24.

A total of 722 adult subjects with chronic rhinosinusitis with nasal polyposis (CRSsNP) were evaluated in 2 randomized, placebo-controlled, multicenter trials of 24 to 52 weeks duration (CSNP Trials 1 and 2). The safety pool consisted of data from the first 24 weeks of treatment from both studies.

In the safety pool, the proportion of subjects who discontinued treatment due to adverse events was 5% of the placebo group and 2% of the DUPIXENT 300 mg Q2W group.

Table 4 summarizes the adverse reactions that occurred at a rate of at least 1% in subjects treated with DUPIXENT and at a higher rate than in their respective comparator groups in CSNP Trials 1 and 2.

Table 4: Adverse Reactions Occurring in ≥1% of the DUPIXENT Group in CRSsNP Trials 1 and 2 and Greater than Placebo (24 Week Safety Pool)

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>DUPIXENT 300 mg Q2W</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injection site reactions</td>
<td>28 (6%)</td>
<td>12 (4%)</td>
</tr>
</tbody>
</table>
Specific Adverse Reactions

The safety profile of DUPIXENT through Week 52 was generally consistent with the safety profile observed at Week 24.

Conjunctivitis

During the 52-week treatment period of concomitant therapy with corticosteroids in atopic dermatitis (Trial 3), conjunctivitis was reported in 16% of the DUPIXENT 300 mg Q2W + TCS group (20 per 100 subject-years) and in 9% of the placebo + TCS group (10 per 100 subject-years). Among asthma subjects, the frequency of conjunctivitis was similar between DUPIXENT and placebo. In the 52-week CSNWP study (CSNP Trial 2), the frequency of conjunctivitis was 3% in the DUPIXENT subjects and 1% in the placebo subjects; all of these subjects recovered. [see Warnings and Precautions (5.2)].

Hypersensitivity Reactions

Hypersensitivity reactions were reported in <1% of DUPIXENT-treated subjects. These included serum sickness reaction, serum sickness-like reaction, generalized urticaria, angioedema, conjunctivitis, conjunctivitis-like reactions, vasculitis, gout, arthritis, arthralgia, and non-fatal strokes. In subjects with CRSwNP, the mean and median increases in blood eosinophil counts compared to treated subjects with placebo. In subjects with atopic dermatitis, the mean and median increases in blood eosinophils from baseline to Week 4 were 100 and 0 cells/μL respectively. In subjects with asthma, the mean and median increases in blood eosinophils from baseline to Week 4 were 130 and 10 cells/μL respectively. In subjects with CRSwNP, the mean and median increases in blood eosinophils from baseline to Week 16 were 150 and 50 cells/μL respectively. Across all indications, the incidence of treatment-emergent eosinophilia (≥500 cells/μL) was similar in DUPIXENT and placebo groups. Treatment-emergent eosinophilia (≥500 cells/μL) was reported in <2% of DUPIXENT-treated patients and <0.5% in placebo-treated patients. Blood eosinophil counts returned to baseline levels during study treatment [see Warnings and Precautions (5.2)].

Cardiovascular

In the 1-year placebo controlled trial in subjects with asthma (AS Trial 2), cardiovascular thromboembolic events (cardiovascular deaths, non-fatal myocardial infarctions, and non-fatal strokes) were reported in 1 (0.2%) of the DUPIXENT 200 mg Q2W group, 4 (0.6%) of the DUPIXENT 300 mg Q2W group, and 2 (0.3%) of the placebo group. In the 1-year placebo controlled trial in subjects with atopic dermatitis (Trial 3), cardiovascular thromboembolic events (cardiovascular deaths, non-fatal myocardial infarctions, and non-fatal strokes) were reported in 1 (0.9%) of the DUPIXENT + TCS 300 mg Q2W group, 0 (0.0%) of the placebo + TCS group, and 1 (0.3%) of the placebo + TCS group.

In the 24-week placebo controlled trial in subjects with CRSwNP (CSNP Trial 1), cardiovascular thromboembolic events (cardiovascular deaths, non-fatal myocardial infarctions, and non-fatal strokes) were reported in 1 (0.7%) of the DUPIXENT group and 0 (0.0%) of the placebo group. In the 1-year placebo controlled trial in subjects with CRSwNP (CSNP Trial 2), there were no cases of cardiovascular thromboembolic events (cardiovascular deaths, non-fatal myocardial infarctions, and non-fatal strokes) reported in any treatment arm.

6.2 Immunogenicity

As with all therapeutic proteins, there is a potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay, as well as variability in assay methodology.

Table 4: Adverse Reactions Occurring in ≥1% of the DUPIXENT Group in CRSwNP Trials 1 and 2 and Greater than Placebo (24 Week Safety Pool) (continued)

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>CSNP Trials 1 and 2</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DUPIXENT</strong></td>
<td><strong>N=440</strong></td>
<td><strong>N=282</strong></td>
</tr>
<tr>
<td><strong>300 mg Q2W</strong></td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>7 (2%)</td>
<td>2 (1%)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>14 (3%)</td>
<td>5 (2%)</td>
</tr>
<tr>
<td>Gastritis</td>
<td>7 (2%)</td>
<td>2 (1%)</td>
</tr>
<tr>
<td>Insomnia</td>
<td>6 (1%)</td>
<td>0 (&lt;1%)</td>
</tr>
<tr>
<td>Eosinophilia</td>
<td>5 (1%)</td>
<td>1 (&lt;1%)</td>
</tr>
<tr>
<td>Toothache</td>
<td>5 (1%)</td>
<td>1 (&lt;1%)</td>
</tr>
</tbody>
</table>

a Injection site reactions cluster includes injection site reaction, pain, bruising and swelling.

b Conjunctivitis cluster includes conjunctivitis, allergic conjunctivitis, bacterial conjunctivitis, viral conjunctivitis, giant papillary conjunctivitis, eye irritation, and eye inflammation.

Additionaly, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors, including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to dupilumab in the studies described below with the incidence of antibodies in other studies or to other products may be misleading.

Approximately 5% of subjects with atopic dermatitis, asthma, or CRSwNP who received DUPIXENT 300 mg Q2W for 52 weeks developed antibodies to dupilumab; approximately 2% exhibited persistent ADA responses, and approximately 2% had neutralizing antibodies.

Approximately 9% of subjects with asthma who received DUPIXENT 200 mg Q2W for 52 weeks developed antibodies to dupilumab; approximately 4% exhibited persistent ADA responses, and approximately 4% had neutralizing antibodies.

Approximately 4% of subjects in the placebo groups in the 52-week studies were positive for antibodies to DUPIXENT; approximately 2% exhibited persistent ADA responses, and approximately 1% had neutralizing antibodies.

Approximately 16% of adolescents with atopic dermatitis who received DUPIXENT 300 mg or 200 mg Q2W for 16 weeks developed antibodies to dupilumab; approximately 3% exhibited persistent ADA responses, and approximately 5% had neutralizing antibodies.

Approximately 4% of adolescent subjects with atopic dermatitis in the placebo group were positive for antibodies to DUPIXENT; approximately 1% exhibited persistent ADA responses, and approximately 1% had neutralizing antibodies.

The antibody titers detected in both DUPIXENT and placebo subjects were mostly low. In subjects receiving DUPIXENT, the detection of duplumab was associated with lower serum dupilumab concentrations [see Clinical Pharmacology (12.3)].

Two subjects who experienced high titer antibody responses developed serum sickness or serum sickness-like reactions during DUPIXENT therapy [see Warnings and Precautions (5.1)].

7 DRUG INTERACTIONS

7.1 Live Vaccines

Avoid use of live vaccines in patients treated with DUPIXENT.

7.2 Non-Live Vaccines

Immune responses to vaccination were assessed in a study in which subjects with atopic dermatitis were treated once weekly for 16 weeks with 300 mg of dupilumab (twice the recommended dosing frequency). After 12 weeks of DUPIXENT administration, subjects were vaccinated with a Tdap vaccine (Adacel®) and a meningococcal polysaccharide vaccine (Menomune®). Antibody responses to tetanus toxoid and serogroup C meningococcal polysaccharide were assessed 4 weeks later. Antibody responses to both tetanus vaccine and meningococcal polysaccharide vaccine were similar in dupilumab-treated and placebo-treated subjects. Immune responses to the other active components of the Adacel and Menomune vaccines were not assessed.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to DUPIXENT during pregnancy. Please contact 1-877-311-8972 or go to https://mothertobaby.org/ongoing-study/dupixent/ to enroll in or to obtain information about the registry.

Risk Summary

Available data from case reports and case series with DUPIXENT use in pregnant women have not identified a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Human IgG antibodies are known to cross the placental barrier; therefore, DUPIXENT may be transmitted from the mother to the developing fetus. There are adverse effects on maternal and fetal outcomes associated with asthma in pregnancy [see Clinical Considerations]. In an enhanced pre- and post-natal development study, no adverse developmental effects were observed in offspring born to pregnant monkeys after subcutaneous administration of a homologous antibody against interleukin-4-receptor alpha (IL-4Rα) during organogenesis through parturition at doses up to 10-times the maximum recommended human dose (MRHD) [see Data]. The estimated background risk of major birth defects and miscarriage for the indicated populations are unknown. All pregnancies have a background risk of birth defect, loss or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations

Disease-Associated Maternal and/or Embryo-fetal Risk

In women with poorly or moderately controlled asthma, evidence demonstrates that there is an increased risk of preterm birth in the mother and prematurity, low birth weight, and small for gestational age in the neonate. The level of asthma control should be closely monitored in pregnant women and treatment adjusted as necessary to maintain optimal control.

Data

Animal Data

In an enhanced pre- and post-natal development toxicity study, pregnant cynomolgus monkeys were administered weekly subcutaneous doses of homologous antibody against IL-4Rα up to 10 times the MRHD (on a mg/kg basis of 100 mg/kg/week) from the beginning of organogenesis to parturition. No treatment-related adverse effects on embryo-fetal toxicity or malformations, or on morphological, functional, or immunological development were observed in the infants from birth through 6 months of age.
2.8 Lactation

Risk Summary

There are no data on the presence of dupilumab in human milk, the effects on the breastfed infant, or the effects on milk production. Maternal IgG is known to be present in human milk. The effects of local gastrointestinal exposure and limited systemic exposure to dupilumab on the breastfed infant are unknown. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for DUXPENX and any potential adverse effects on the breastfed child from DUXPENX or from the underlying maternal condition.

8.4 Pediatric Use

Aortic Dermatitis

The safety and efficacy of DUXPENX have been established in pediatric patients 12 years of age and older with moderate-to-severe aortic dermatitis. A total of 251 adolescents ages 12 to 17 years old with moderate-to-severe aortic dermatitis were enrolled in Trial 6. The safety and efficacy were generally consistent between adolescents and adults [see Adverse Reactions (6.1) and Clinical Studies (14.1)]. Safety and efficacy in pediatric patients (<12 years of age) with aortic dermatitis have not been established.

Asthma

A total of 107 adolescents aged 12 to 17 years with moderate-to-severe asthma were enrolled in AS Trial 2 and received either 200 mg (N=21) or 300 mg (N=18) DUXPENX (or matching placebo) either 200 mg (N=34) or 300 mg (N=34) Q2W. Asthma exacerbations and lung function were assessed in both adolescents and adults. For both the 200 mg and 300 mg Q2W doses, improvements in FEV<sub>1</sub> (LS mean change from baseline at Week 12) were observed (0.36 L and 0.27 L, respectively). For the 200 mg Q2W dose, subjects had a reduction in the rate of severe exacerbations that was consistent with adults. Safety and efficacy in pediatric patients (<12 years of age) with asthma have not been established. Dupilumab exposure was higher in adolescent patients than in adults at the respective dose level which was mainly accounted for by difference in body weight [see Clinical Pharmacology (12.3)]. The adverse event profile in adolescents was generally similar to the adults [see Adverse Reactions (6.1)].

CRSwNP

CRSwNP does not normally occur in children. Safety and efficacy in pediatric patients (<18 years of age) with CRSwNP have not been established.

8.5 Geriatric Use

Of the 1472 subjects with atopic dermatitis exposed to DUXPENX in a dose-ranging study and placebo-controlled trials, 67 subjects were 65 years or older. Although no differences in safety or efficacy were observed between older and younger subjects, the number of subjects aged 65 and over is not sufficient to determine whether they respond differently from younger subjects [see Clinical Pharmacology (12.3)]. Of the 177 subjects with asthma exposed to DUXPENX, a total of 240 subjects were 65 years or older. Efficacy and safety in this age group was similar to the overall study population. Of the 440 subjects with CRSwNP exposed to DUXPENX, a total of 79 subjects were 65 years or older. Efficacy and safety in this age group were similar to the overall study population.

10 OVERDOSE

There is no specific treatment for DUXPENX overdose. In the event of overdosage, monitor the patient for any signs or symptoms of adverse reactions and institute appropriate symptomatic treatment immediately.

11 DESCRIPTION

Dupliclumab, an interleukin-4 receptor alpha antagonist, is a human monoclonal antibody of the IgG4 subclass that binds to the IL-4 receptor subunit and inhibits IL-4 and IL-13 signaling. Dupliclumab has an approximate molecular weight of 147 kDa.

Dupliclumab is produced by recombinant DNA technology in Chinese Hamster Ovary cell suspension culture.

DUXPENX (dupilumab) Injection is supplied as a sterile, preservative-free, clear to slightly opalescent, colorless to pale yellow solution for subcutaneous injection. DUXPENX is provided as a single-dose pre-filled syringe with needle shield in a siliconized Type-1 clear glass syringe. The needle cap is not made with natural rubber latex.

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dose of 600 mg followed by 300 mg SC weekly for six weeks). No clinically significant changes in AUC were observed. The largest effect was observed for metoprolol (CYP2D6) with an increase in AUC of 29%.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Animal studies have not been conducted to evaluate the carcinogenic or mutagenic potential of dupilumab.

No effects on fertility parameters such as reproductive organs, menstrual cycle length, or sperm analysis were observed in sexually mature mice that were subcutaneously administered a homologous antibody against IL-4Rx at doses up to 200 mg/kg/week.

14 CLINICAL STUDIES

14.1 Atopic Dermatitis

Adults with Atopic Dermatitis

Three randomized, double-blind, placebo-controlled trials (Trials 1, 2, and 3; NCT02277743, 02277769, and 02260986 respectively) enrolled a total of 2119 subjects 18 years of age and older with moderate-to-severe atopic dermatitis (AD) not adequately controlled by topical medication(s). Disease severity was defined by an Investigator’s Global Assessment (IGA) score ≥3 in the overall assessment of AD lesions on a severity scale of 0 to 4, an Eczema Area and Severity Index (EASI) score ≥16 on a scale of 0 to 72, and a minimum body surface area involvement of ≥10%. At baseline, 59% of subjects were male, 67% were white, 52% of subjects had a baseline IGA score of 3 (moderate AD), and 48% of subjects had a baseline IGA of 4 (severe AD). The baseline mean EASI score was 33 and the baseline weekly averaged Peak Pruritus Numeric Rating Scale (NRS) was 7 on a scale of 0-10.

In all three trials, subjects in the DUPIXENT group received subcutaneous injections of DUXIPENT 600 mg at Week 0, followed by 300 mg every other week (Q2W). In the monotherapy trials (Trials 1 and 2), subjects received DUPIXENT or placebo for 16 weeks.

In the concomitant therapy trial (Trial 3), subjects received DUPIXENT or placebo with concomitant topical corticosteroids (TCS) and as needed topical calcineurin inhibitors for problem areas only, such as the face, neck, intertriginous and genital areas for 52 weeks.

All three trials assessed the primary endpoint, the change from baseline to Week 16 in AD severity as defined by an Investigator’s Global Assessment (IGA) score ≥0 or 1 (clear or almost clear) and a reduction of ≥2 points on a 0-4 IGA scale.

Clinical Response at Week 16 (Trials 1, 2, and 3)

The results of the DUPIXENT monotherapy trials (Trials 1 and 2) and the DUPIXENT with concomitant TCS trial (Trial 3) are presented in Table 5.

Table 5: Efficacy Results of DUPIXENT With or Without Concomitant TCS at Week 16 (FAS)

<table>
<thead>
<tr>
<th></th>
<th>Trial 1</th>
<th>Trial 2</th>
<th>Trial 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DUPIXENT 300 mg</td>
<td>Placebo + TCS</td>
<td>Placebo + TCS</td>
</tr>
<tr>
<td></td>
<td>Q2W</td>
<td>DUPIXENT 300 mg</td>
<td>DUPIXENT 300 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Q2W</td>
<td>Q2W + TCS</td>
</tr>
<tr>
<td>Number of subjects randomized (FAS)</td>
<td>224</td>
<td>233</td>
<td>106</td>
</tr>
<tr>
<td>IGA 0 or 1b,c</td>
<td>38%</td>
<td>36%</td>
<td>39%</td>
</tr>
<tr>
<td>EASI-75b</td>
<td>51%</td>
<td>44%</td>
<td>69%</td>
</tr>
<tr>
<td>EASI-90b</td>
<td>36%</td>
<td>30%</td>
<td>40%</td>
</tr>
<tr>
<td>Number of subjects with baseline Peak Pruritus NRS score ≥4</td>
<td>213</td>
<td>225</td>
<td>102</td>
</tr>
<tr>
<td>Peak Pruritus NRS score ≥4 (2-point improvement)</td>
<td>41%</td>
<td>36%</td>
<td>59%</td>
</tr>
</tbody>
</table>

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 non-responders.

Table 6: Efficacy Results (IGA 0 or 1) of DUPIXENT with Concomitant TCS at Week 16 and 52

<table>
<thead>
<tr>
<th></th>
<th>DUPIXENT 300 mg Q2W + TCS</th>
<th>Placebo + TCS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Subjects</td>
<td>89</td>
<td>264</td>
</tr>
<tr>
<td>Responderb,c at Week 16 and 52</td>
<td>22%</td>
<td>7%</td>
</tr>
<tr>
<td>Responder at Week 16 but Non-respondent at Week 52</td>
<td>20%</td>
<td>7%</td>
</tr>
<tr>
<td>Non-responder at Week 16 and Non-respondent at Week 52</td>
<td>13%</td>
<td>6%</td>
</tr>
<tr>
<td>Non-responder at Week 16 and 52</td>
<td>44%</td>
<td>80%</td>
</tr>
<tr>
<td>Overall Responderb,c Rate at Week 52</td>
<td>36%</td>
<td>13%</td>
</tr>
</tbody>
</table>

a. In Trial 3, of the 421 randomized and treated subjects, 68 subjects (16%) had not been on study for 52 weeks at the time of data analysis.
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 non-responders.

Treatment effects in subgroups (weight, age, gender, race, and prior treatment, including immunosuppressants) in Trials 1, 2, and 3 were generally consistent with the results in the overall study population.

In Trials 1, 2, and 3, a third randomized treatment arm of DUPIXENT 300 mg Q2W did not demonstrate additional treatment benefit over DUPIXENT 300 mg Q2W. Subjects in Trials 1 and 2 who had an IGA 0 or 1 with a reduction of ≥2 points were re-randomized into Trial 5. Trial 5 evaluated multiple DUPIXENT monotherapy dose regimens for maintaining treatment response. The study included subjects randomized to continue with DUPIXENT 300 mg Q2W (62 subjects) or switch to placebo (51 subjects) for 36 weeks. IGA 0 or 1 responses at Week 36 were as follows: 33 (53%) in the Q2W group and 3 (10%) in the placebo group.

Adolescents with Atopic Dermatitis

The efficacy and safety of DUPIXENT monotherapy in adolescent subjects was evaluated in a multicenter, randomized, double-blind, placebo-controlled trial (Trial 6; NCT03054428) in 251 adolescent subjects 12 to 17 years of age, with moderate-to-severe AD defined by an IGA score ≥3 (scale of 0 to 72), an EASI score ≥16 (scale of 0 to 72), and a minimum BSA involvement of ≥10%. Eligible subjects enrolled into this trial had previous inadequate response to topical medication.

Subjects in the DUPIXENT group with baseline weight of <60 kg received an initial dose of 400 mg at Week 0, followed by 200 mg Q2W for 16 weeks. Subjects with baseline weight of ≥60 kg received an initial dose of 800 mg at Week 0, followed by 300 mg Q2W for 16 weeks. Subjects were permitted to receive rescue treatment at the discretion of the investigator. Subjects who received rescue treatment were considered non-responders.

In Trial 6, the mean age was 14.5 years, the median weight was 59.4 kg, 41% of subjects were female, 63% were White, 15% were Asian, and 12% were Black. Baseline 46% of subjects had an IGA score of 3 (moderate AD), 54% had an IGA score of 4 (severe AD), the mean BSA involvement was 57%, and 42% had received prior systemic immunosuppressants. Also, at baseline the mean EASI score was 36, and the weekly averaged Peak Pruritus NRS was 8 on a scale of 0-10. Overall, 92% of subjects had at least one concomitant allergic condition; 66% had allergic rhinitis, 54% had asthma, and 61% had food allergies.
The primary endpoint was the proportion of subjects with an IGA 0 (clear) or 1 (almost clear) and at least a 2-point improvement from baseline to Week 16. Other outcomes included the proportion of subjects with EASI-75 or EASI-90 (improvement of at least 75% or 90% in EASI from baseline, respectively), and reduction in itch as measured by the Peak Pruritus NRS (≥4-point improvement).

The efficacy results at Week 16 for Trial 6 are presented in Table 7.

Table 7: Efficacy Results of DUPIXENT in Trial 6 at Week 16 (FAS)*

<table>
<thead>
<tr>
<th>Parameter</th>
<th>DUPIXENT&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Placebo&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>200 mg (&lt;300 kg) Q2W</td>
<td>200 mg (&lt;300 kg) Q2W</td>
<td>N=85</td>
</tr>
<tr>
<td>300 mg (&lt;300 kg) Q2W</td>
<td>300 mg (&lt;300 kg) Q2W</td>
<td>N=85</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>N</th>
<th>IGA 0 or 1&lt;sup&gt;a&lt;/sup&gt;</th>
<th>EASI-75&lt;sup&gt;b&lt;/sup&gt;</th>
<th>EASI-90&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Peak Pruritus NRS (≥4-point improvement)&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=157</td>
<td>24%</td>
<td>42%</td>
<td>23%</td>
<td>37%</td>
<td></td>
</tr>
<tr>
<td>N=160</td>
<td>2%</td>
<td>8%</td>
<td>2%</td>
<td>5%</td>
<td></td>
</tr>
</tbody>
</table>

* 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.

A greater proportion of subjects randomized to DUPIXENT achieved an improvement in the Peak Pruritus NRS compared to placebo (defined as ≥4-point improvement at Week 4). See Figure 2.

Figure 2: Proportion of Adolescent Subjects with ≥4-point Improvement on the Peak Pruritus NRS in Trial 6<sup>d</sup> (FAS)<sup>b</sup>

a In the primary analyses of the efficacy endpoints, subjects who received rescue treatment or with missing data were considered non-responders.

b Full Analysis Set (FAS) includes all subjects randomized.

14.2 Asthma

The asthma development program included three randomized, double-blind, placebo-controlled, parallel-group, multi-center trials (AS Trials 1, 2, and 3) of 24 to 52 weeks in treatment duration which enrolled a total of 2888 subjects (12 years of age and older). Subjects enrolled in AS Trials 1 and 2 were required to have a history of 1 or more asthma exacerbations that required treatment with systemic corticosteroids or emergency department visit or hospitalization for the treatment of asthma in the year prior to trial entry. Subjects enrolled in AS Trial 3 required dependence on daily oral corticosteroids in addition to regular use of high-dose inhaled corticosteroids plus an additional controller(s). In all 3 trials, subjects were enrolled without requiring a minimum baseline blood eosinophil count. In AS Trials 2 and 3 subjects with screening blood eosinophil level of >1500 cells/μL (<1.3%) were excluded. DUPIXENT was administered as add-on to background asthma treatment. Subjects continued background asthma therapy throughout the duration of the studies, except in AS Trial 3 in which OCS dose was tapered as described below.

AS Trial 1

AS Trial 1 was a 24-week dose-ranging study which included 776 subjects (18 years of age and older). DUPIXENT compared with placebo was evaluated in adult subjects with moderate-to-severe asthma on a medium or high-dose inhaled corticosteroid (ICS) and a minimum of one or up to two additional controller medications. Subjects were randomized to receive either 200 mg (N=631) or 300 mg (N=633) DUPIXENT Q2W (or matching placebo for either 200 mg [N=317] or 300 mg [N=321] Q2W) following an initial dose of 400 mg, 600 mg or placebo respectively. The primary endpoints were the annualized rate of severe exacerbation events during the 52-week placebo controlled period and change from baseline in pre-bronchodilator FEV1, at Week 12 in the overall population (unrestricted by minimum baseline blood eosinophil count). Additional secondary endpoints included annualized severe exacerbation rates and FEV1 in patients with different baseline levels of blood eosinophils as well as responder rates in the ACQ-5 and AQLQ(S) scores.

AS Trial 2

AS Trial 2 was a 52-week study which included 1902 subjects (12 years of age and older). DUPIXENT compared with placebo was evaluated in 1074 adolescent and 775 adult subjects with moderate-to-severe asthma on a medium or high-dose inhaled corticosteroid (ICS) and a minimum of one and up to two additional controller medications. Subjects were randomized to receive either 200 mg (N=631) or 300 mg (N=633) DUPIXENT Q2W (or matching placebo for either 200 mg [N=317] or 300 mg [N=321] Q2W) following an initial dose of 400 mg, 600 mg or placebo respectively. The primary endpoints were the annualized rate of severe exacerbation events during the 52-week placebo controlled period and change from baseline in pre-bronchodilator FEV1, at Week 12 in the overall population (unrestricted by minimum baseline blood eosinophil count). Additional secondary endpoints included annualized severe exacerbation rates and FEV1 in patients with different baseline levels of blood eosinophils as well as responder rates in the ACQ-5 and AQLQ(S) scores.

AS Trial 3

AS Trial 3 was a 24-week oral corticosteroid-reduction study in 210 subjects with asthma who required daily oral corticosteroids in addition to regular use of high-dose inhaled corticosteroids plus an additional controller. After optimizing the OCS dose during the screening period, subjects received 300 mg DUPIXENT (N=103) or placebo (N=107) once Q2W for 24 weeks following an initial dose of 600 mg or placebo. Subjects continued to receive their existing asthma medicine during the study; however their OCS dose was reduced every 4 weeks during the OCS reduction phase (Week 4-20), as long as asthma control was maintained. The primary endpoint was the percent reduction of oral corticosteroid dose at Weeks 20 to 24 compared with the baseline dose, while maintaining asthma control in the overall population (unrestricted by minimum baseline blood eosinophil count). Additional secondary endpoints included the annualized rate of severe exacerbation events during treatment period and responder rate in the ACQ-5 and AQLQ(S) scores.

The demographics and baseline characteristics of these 3 trials are provided in Table 8 below.

Table 8: Demographics and Baseline Characteristics of Asthma Trials

<table>
<thead>
<tr>
<th>Parameter</th>
<th>AS Trial 1 (N=776)</th>
<th>AS Trial 2 (N=1902)</th>
<th>AS Trial 3 (N=210)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years) (SD)</td>
<td>14.2 (3.5)</td>
<td>14.2 (3.5)</td>
<td>14.2 (3.5)</td>
</tr>
<tr>
<td>% Female</td>
<td>50.1</td>
<td>50.3</td>
<td>50.0</td>
</tr>
<tr>
<td>% White</td>
<td>78.5</td>
<td>78.5</td>
<td>78.5</td>
</tr>
<tr>
<td>Duration of Asthma (years)</td>
<td>22.1 (15)</td>
<td>22.1 (15)</td>
<td>22.1 (15)</td>
</tr>
<tr>
<td>Mean exacerbations prior</td>
<td>2.2 (2.1)</td>
<td>2.2 (2.1)</td>
<td>2.2 (2.1)</td>
</tr>
<tr>
<td>Mean high dose ICS use (%)</td>
<td>77.7</td>
<td>81.0</td>
<td>81.0</td>
</tr>
<tr>
<td>Pre-dose FEV1 (L at baseline)</td>
<td>1.84 (0.54)</td>
<td>1.78 (0.60)</td>
<td>1.58 (0.57)</td>
</tr>
<tr>
<td>Mean percent predicted FEV1 at baseline (%)</td>
<td>61 (11)</td>
<td>58 (14)</td>
<td>52 (15)</td>
</tr>
<tr>
<td>% Reversibility (%)</td>
<td>27 (15)</td>
<td>26 (22)</td>
<td>19 (23)</td>
</tr>
<tr>
<td>Atopic Medical History %</td>
<td>73 (8, 11, 62)</td>
<td>78 (10, 13, 69)</td>
<td>72 (8, 21, 56)</td>
</tr>
<tr>
<td>Mean FeNO ppb (± SD)</td>
<td>39 (35)</td>
<td>35 (33)</td>
<td>38 (31)</td>
</tr>
<tr>
<td>Mean baseline blood Eosinophil count (± SD) cells/μL</td>
<td>350 (430)</td>
<td>360 (370)</td>
<td>350 (310)</td>
</tr>
</tbody>
</table>

ICS = inhaled corticosteroid; FEV1 = Forced expiratory volume in 1 second; AD = atopic dermatitis; NP = nasal polypsis; AR = allergic rhinitis; FeNO = fraction of exhaled nitric oxide

Exacerbations

AS Trials 1 and 2 evaluated the frequency of severe asthma exacerbations defined as deterioration of asthma requiring the use of systemic corticosteroids for at least 3 days or hospitalization or emergency room visit due to asthma that required systemic corticosteroids. In the primary analysis population (subjects with baseline blood eosinophil count of ≥300 cells/μL in AS Trial 1 and the overall population in AS Trial 2), subjects receiving either DUPIXENT 200 mg or 300 mg Q2W had significant reductions in the rate of asthma exacerbations compared to placebo. In the overall population in AS Trial 2, the rate of severe exacerbations was 0.46 and 0.52 for DUPIXENT 200 mg Q2W and 300 mg 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 200 mg Q2W and 300 mg Q2W, respectively. Results in subjects with baseline blood eosinophil counts ≥300 cells/μL in AS Trials 1 and 2 are shown in Table 9.

Response rates by baseline blood eosinophils for AS Trial 2 are shown in Figure 3. Pre-specified subgroup analyses of AS Trials 1 and 2 demonstrated that there were greater reductions in severe exacerbations in subjects with higher baseline blood eosinophil levels. In AS Trial 2, reductions in exacerbations were significant in the subgroup of subjects with baseline blood eosinophils ≥150 cells/μL. In subjects with
baseline blood eosinophil count <150 cells/mL, similar severe exacerbation rates were observed between DUPIXENT and placebo.

In AS Trial 2, the estimated rate ratio of exacerbations leading to hospitalizations and/or emergency room visits versus placebo was 0.53 (95% CI: 0.28, 1.00) and 0.74 (95% CI: 0.32, 1.70) with DUPIXENT 200 mg or 300 mg Q2W, respectively.

Table 9: Rate of Severe Exacerbations in AS Trials 1 and 2

<table>
<thead>
<tr>
<th>Trial</th>
<th>Treatment</th>
<th>Baseline Blood EOS ≥300 cells/mL (primary analysis population, Trial 1)</th>
<th>N</th>
<th>Rate (95% CI)</th>
<th>Rate Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AS Trial 1</td>
<td>DUPIXENT 200 mg Q2W</td>
<td>65</td>
<td>0.30 (0.13, 0.68)</td>
<td>0.29 (0.11, 0.76)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>DUPIXENT 300 mg Q2W</td>
<td>64</td>
<td>0.20 (0.08, 0.52)</td>
<td>0.19 (0.07, 0.56)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>68</td>
<td>1.04 (0.57, 1.90)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AS Trial 2</td>
<td>DUPIXENT 200 mg Q2W</td>
<td>264</td>
<td>0.37 (0.29, 0.48)</td>
<td>0.34 (0.24, 0.48)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>148</td>
<td>1.08 (0.85, 1.38)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>DUPIXENT 300 mg Q2W</td>
<td>277</td>
<td>0.40 (0.32, 0.51)</td>
<td>0.33 (0.23, 0.45)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>142</td>
<td>1.24 (0.97, 1.57)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The time to first exacerbation was longer for the subjects receiving DUPIXENT compared to placebo in AS Trial 2 (Figure 4).

Figure 3: Relative Risk in Annualized Event Rate of Severe Exacerbations across Baseline Blood Eosinophil Counts (cells/mL) in AS Trial 2

The ACQ-5 responder rate for DUPIXENT 200 mg and 300 mg Q2W in subjects with baseline blood eosinophil counts ≥300 cells/mL was 75% vs 67% placebo (odds ratio: 1.46; 95% CI: 0.90, 2.35) and 71% vs 64% placebo (odds ratio: 1.39; 95% CI: 0.88, 2.19), respectively; and the AQLQ(S) responder rates were 71% vs 55% placebo (odds ratio: 1.61; 95% CI: 1.17, 2.21) and 62% vs 57% placebo (odds ratio: 1.33; 95% CI: 0.98, 1.81), respectively.

Table 10: Mean Change from Baseline and vs Placebo in Pre-Bronchodilator FEV1, at Week 12 in AS Trials 1 and 2

<table>
<thead>
<tr>
<th>Trial</th>
<th>Treatment</th>
<th>Baseline Blood EOS ≥300 cells/mL (primary analysis population, Trial 1)</th>
<th>N</th>
<th>LS Mean Change from baseline</th>
<th>LS Mean Difference vs placebo (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AS Trial 1</td>
<td>DUPIXENT 200 mg Q2W</td>
<td>65</td>
<td>0.43 (25.9)</td>
<td>0.26 (0.11, 0.40)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>DUPIXENT 300 mg Q2W</td>
<td>64</td>
<td>0.39 (25.8)</td>
<td>0.21 (0.06, 0.36)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>68</td>
<td>0.18 (10.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AS Trial 2</td>
<td>DUPIXENT 200 mg Q2W</td>
<td>264</td>
<td>0.43 (29.0)</td>
<td>0.21 (0.13, 0.29)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>148</td>
<td>0.21 (15.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>DUPIXENT 300 mg Q2W</td>
<td>277</td>
<td>0.47 (32.5)</td>
<td>0.24 (0.14, 0.32)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>142</td>
<td>0.22 (14.4)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Mean changes in FEV1 over time in AS Trial 2 are shown in Figure 6.

Figure 4: Kaplan Meier Incidence Curve for Time to First Severe Exacerbation in Subjects with Baseline Blood Eosinophils ≥300 cells/mL (AS Trial 2)

Lung Function

Significant increases in pre-bronchodilator FEV1 were observed at Week 12 for AS Trials 1 and 2 in the primary analysis populations (subjects with baseline blood eosinophil count of ≥300 cells/mL in AS Trial 1 and the overall population in AS Trial 2). In the overall population in AS Trial 2, the FEV1 LS mean change from baseline was 0.32 L (21%) and 0.34 L (23%) for DUPIXENT 200 mg Q2W and 300 mg Q2W, respectively, compared to matched placebo means of 0.18 L (12%) and 0.21 L (14%). The mean treatment difference versus placebo was 0.14 L (95% CI: 0.08, 0.19) and 0.13 L (95% CI: 0.08, 0.18) for DUPIXENT 200 mg Q2W and 300 mg Q2W, respectively. Results in subjects with baseline blood eosinophil counts ≥300 cells/mL in AS Trials 1 and 2 are shown in Table 10. Improvements in FEV1, by baseline blood eosinophils for AS Trial 2 are shown in Figure 5. Subgroup analysis of AS Trials 1 and 2 demonstrated greater improvement in subjects with higher baseline blood eosinophils.

Additional Secondary Endpoints

ACQ-5 and AQLQ(S) were assessed in AS Trial 2 at 52 weeks. The responder rate was defined as an improvement in score of 0.5 or more (scale range 0-6 for ACQ-5 and 1-7 for AQLQ(S)).

- The ACQ-5 responder rate for DUPIXENT 200 mg and 300 mg Q2W in the overall population was 69% vs 62% placebo (odds ratio 1.37; 95% CI: 1.01, 1.86) and 69% vs 63% placebo (odds ratio 1.28; 95% CI: 0.94, 1.73), respectively; and the AQLQ(S) responder rates were 62% vs 54% placebo (odds ratio 1.18; 95% CI: 1.00, 1.38) and 65% vs 55% placebo (odds ratio 1.39; 95% CI: 0.88, 2.19), respectively.

Oral Corticosteroid Reduction (AS Trial 3)

AS Trial 3 evaluated the effect of DUPIXENT on reducing the use of maintenance oral corticosteroids. The baseline mean oral corticosteroid dose was 12 mg in the placebo group and 11 mg in the group receiving DUPIXENT. The primary endpoint was the percent reduction from baseline of the final oral corticosteroid dose at Week 24 while maintaining asthma control.
Compared with placebo, subjects receiving DUXIPENT achieved greater reductions in daily maintenance oral corticosteroid dose, while maintaining asthma control. The mean percent reduction in daily oral corticosteroid dose from baseline was 70% (median 100%) in subjects receiving DUXIPENT (95% CI: 60%, 80%) compared to 42% (median 50%) in subjects receiving placebo (95% CI: 33%, 51%). Reductions of 50% or higher in the OCS dose were observed in 80% (80%) subjects receiving DUXIPENT compared to 57% (53%) in those receiving placebo. The proportion of subjects with a mean final dose less than 5 mg was higher in those receiving DUXIPENT. Weeks 24 was 72% for DUXIPENT and 37% for placebo (odds ratio 4.48 95% CI: 2.39, 8.39). A total of 54 (52%) subjects receiving DUXIPENT versus 31 (29%) subjects in the placebo group had a 100% reduction in their OCS dose.

In this 24-week trial, asthma exacerbations (defined as a temporary increase in oral corticosteroid dose for at least 3 days) were lower in subjects receiving DUXIPENT compared with those receiving placebo (annualized rate 0.65 and 1.60 for the DUXIPENT and placebo group, respectively; rate ratio 0.41 [95% CI 0.26, 0.63]) and improvement in pre-bronchodilator FEV1, from baseline to Week 24, was greater in subjects receiving DUXIPENT compared with those receiving placebo (LS mean difference for DUXIPENT versus placebo of 0.22 L [95% CI: 0.09 to 0.34 L]). Effects on lung function and on oral steroid and exacerbation reduction were similar irrespective of baseline blood eosinophil levels. The ACOG-S and AQLQ(S) were also assessed in AS Trial 3 and showed improvements similar to those in AS Trial 2.

### 14.3 Chronic Rhinosinusitis with Nasal Polyposis

The chronic rhinosinusitis with nasal polyposis (CRSwNP) development program included two randomized, double-blind, parallel-group, multicenter, placebo-controlled studies (CSNP Trial 1 and CSNP Trial 2) in 724 subjects aged 18 years and older on background intranasal corticosteroids (INCS). These studies included subjects with CRSwNP despite prior sino-nasal surgery or treatment with, or who were ineligible to receive or were intolerant to, systemic corticosteroids in the past 2 years. Patients with chronic rhinosinusitis without nasal polyposis were not included in these trials. Rescue with systemic corticosteroids or surgery was allowed during the studies at the investigator’s discretion. In CSNP Trial 1, a total of 276 subjects were randomized to receive either 300 mg DUXIPENT (N=143) or placebo (N=133) every other week for 24 weeks. In CSNP Trial 2, 448 subjects were randomized to receive either 300 mg DUXIPENT (N=150) or placebo (N=153) every other week for 52 weeks. 300 mg DUXIPENT (N=145) every other week until week 24 followed by 300 mg DUXIPENT every 4 weeks until week 52, or placebo (N=153). All subjects had evidence of sinonasal opacification on the Lund Mackay (LMK) sinus CT scan and 73% to 90% of subjects had opacification of all sinuses. Subjects were stratified based on their histories of prior surgery and co-morbid asthma/nonsteroidal anti-inflammatory drug exacerbated respiratory disease (NSAID-ERD). A total of 63% of subjects reported previous sinus surgery, with a mean number of 2.0 prior surgeries, 74% used systemic corticosteroids in the previous 2 years with a mean number of 1.6 systemic corticosteroid courses in the previous 2 years, 59% had co-morbid asthma, and 28% had NSAID-ERD.

The co-primary efficacy endpoints were change from baseline to Week 24 in bilateral nasal polyp scores (NPS; 0-8 scale) and percent reduction in daily oral corticosteroid dose from baseline (at least 5 mg at the lower border of the inferior turbinate/polypos medial to the middle turbinate; 4=large polyps causing complete obstruction of the inferior nasal cavity). The total score was the sum of the right and left scores. Nasal congestion was scored daily by the subjects on a 0 to 3 categorical severity scale (0=no symptoms; 1=mild symptoms; 2=moderate symptoms; 3=severe symptoms).

### Table 11: Demographics and Baseline Characteristics of CRSwNP Trials

<table>
<thead>
<tr>
<th>Parameter</th>
<th>CSNP Trial 1 (N=276)</th>
<th>CSNP Trial 2 (N=448)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years) (SD)</td>
<td>50 (13)</td>
<td>52 (12)</td>
</tr>
<tr>
<td>% Male</td>
<td>57</td>
<td>62</td>
</tr>
<tr>
<td>Mean CRSwNP duration (years) (SD)</td>
<td>11 (9)</td>
<td>11 (10)</td>
</tr>
<tr>
<td>Patients with ≥ 1 prior surgery (%)</td>
<td>72</td>
<td>58</td>
</tr>
<tr>
<td>Patients with systemic corticosteroid use in the previous 2 years (%)</td>
<td>65</td>
<td>80</td>
</tr>
<tr>
<td>Mean Basal endoscopic NPS* (SD), range 0-8</td>
<td>5.8 (1.3)</td>
<td>6.1 (1.2)</td>
</tr>
<tr>
<td>Mean Nasal congestion (NC) score* (SD), range 0-3</td>
<td>2.4 (0.6)</td>
<td>2.4 (0.6)</td>
</tr>
<tr>
<td>Mean LMK sinus CT total score* (SD), range 0-24</td>
<td>19 (4.4)</td>
<td>18 (3.8)</td>
</tr>
<tr>
<td>Mean loss of smell score** (AM), range 0-3</td>
<td>2.7 (0.5)</td>
<td>2.8 (0.5)</td>
</tr>
<tr>
<td>Mean SNOT-22 total score* (SD), range 0-110</td>
<td>49.4 (20.2)</td>
<td>51.9 (20.9)</td>
</tr>
<tr>
<td>Mean blood eosinophils (cells/ml) (SD)</td>
<td>440 (330)</td>
<td>430 (350)</td>
</tr>
<tr>
<td>Mean total IgE IU/ml (SD)</td>
<td>212 (276)</td>
<td>240 (342)</td>
</tr>
<tr>
<td>Atopic Medical History % Overall</td>
<td>75%</td>
<td>82%</td>
</tr>
<tr>
<td>Asthma (%)</td>
<td>58</td>
<td>60</td>
</tr>
<tr>
<td>NSAID-ERD (%)</td>
<td>30</td>
<td>27</td>
</tr>
</tbody>
</table>

* SD = standard deviation; AM = morning; NPS = nasal polyps score; SNOT-22 = 22-item sino-nasal outcome test; NSAID-ERD = asthma/nonsteroidal anti-inflammatory drug exacerbated respiratory disease

** Higher scores indicate greater disease severity

Clinical Response (CSNP Trial 1 and CSNP Trial 2):

The results for primary endpoints in CRSwNP studies are presented in Table 12.

### Table 12: Results of the Primary Endpoints in CRSwNP Trials

<table>
<thead>
<tr>
<th>Primary Endpoints at Week 24</th>
<th>Placebo (n=133)</th>
<th>DUXIPENT 300 mg Q2W (n=143)</th>
<th>LS mean difference vs. Placebo (95% CI)</th>
<th>Placebo (n=153)</th>
<th>DUXIPENT 300 mg Q2W (n=265)</th>
<th>LS mean difference vs. Placebo (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NPS</td>
<td>5.86</td>
<td>0.17</td>
<td>-2.06 (-2.43, -1.69)</td>
<td>5.96</td>
<td>0.10</td>
<td>-1.71 (-2.10, -1.51)</td>
</tr>
<tr>
<td>NC</td>
<td>2.45</td>
<td>-0.45</td>
<td>-0.89 (-1.07, -0.71)</td>
<td>2.38</td>
<td>-0.38</td>
<td>-1.25 (-1.03, -0.71)</td>
</tr>
</tbody>
</table>

A reduction in score indicates improvement.

NPS = nasal polyps score; NC = nasal congestion/obstruction
Statistically significant efficacy was observed in CSNP Trial 2 with regard to improvement in bilateral endoscopic NPS score at week 24 and week 52 (see Figure 7).

Figure 7: LS Mean Change from Baseline in Bilateral Nasal Polyps Score (NPS) up to Week 52 in CSNP Trial 2 - ITT Population

At Week 52, the LS mean difference for nasal congestion in the DUPIXENT group versus placebo was -0.98 (95% CI -1.17, -0.79). In both studies, significant improvements in nasal congestion were observed as early as the first assessment at Week 4. The LS mean difference for nasal congestion at Week 4 in the DUPIXENT group versus placebo was -0.41 (95% CI: -0.52, -0.30) in CSNP Trial 1 and -0.37 (95% CI: -0.46, -0.27) in CSNP Trial 2.

A significant increase in the LMK sinus CT scan score was observed. The LS mean difference for LMK sinus CT scan score at Week 24 in the DUPIXENT group versus placebo was -7.44 (95% CI: -8.15, -6.73) in CSNP Trial 1 and -5.13 (95% CI: -5.86, -4.46) in CSNP Trial 2. At Week 52, in CSNP Trial 2 the LS mean difference for LMK sinus CT scan score in the DUPIXENT group versus placebo was -6.94 (95% CI: -7.87, -6.01).

Dupilumab significantly improved the loss of smell compared to placebo. The LS mean difference for loss of smell at Week 24 in the DUPIXENT group versus placebo was -1.12 (95% CI: -1.31, -0.93) in CSNP Trial 1 and -0.98 (95% CI: -1.15, -0.81) in CSNP Trial 2. At Week 52, the LS mean difference for loss of smell in the DUPIXENT group versus placebo was -1.10 (95% CI: -1.31, -0.89). In both studies, significant improvements in daily loss of smell severity were observed as early as the first assessment at Week 4.

Dupilumab significantly decreased sino-nasal symptoms as measured by SNOT-22 compared to placebo. The LS mean difference for SNOT-22 at Week 24 in the DUPIXENT group versus placebo was -21.12 (95% CI: -25.17, -17.06) in CSNP Trial 1 and -17.36 (95% CI: -20.87, -13.85) in CSNP Trial 2. At Week 52, the LS mean difference in the DUPIXENT group versus placebo was -20.96 (95% CI: -25.03, -16.89).

In the pre-specified multiplicity-adjusted pooled analysis of two studies, treatment with DUPLEXINT resulted in significant reduction of systemic corticosteroid use and need for sino-nasal surgery versus placebo (HR of 0.24; 95% CI 0.17, 0.35) (see Figure 9). The proportion of subjects who required systemic corticosteroids was reduced by 74% (HR of 0.26; 95% CI 0.18, 0.38). The total number of systemic corticosteroid courses per year in subjects with co-morbid asthma, improvements in pre-bronchodilator FEV1 were similar to patients in the asthma program.

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

DUPIXENT (dupilumab) Injection is a clear to slightly opalescent, colorless to pale yellow solution, supplied in single-dose pre-filled syringes with needle shield. Each pre-filled syringe with needle shield is designed to deliver either 300 mg of DUPIXENT in 2 mL (NDC 0024-5914-00) or 200 mg of DUPIXENT in 1.14 mL solution (NDC 0024-5918-00).

DUPIXENT is available in cartons containing 2 pre-filled syringes with needle shield.

16.2 Storage and Handling

DUPIXENT is sterile and preservative-free. Discard any unused portion.

Store refrigerated at 36°F to 46°F (2°C to 8°C) in the original carton to protect from light.

If necessary, pre-filled syringes may be kept at room temperature up to 77°F (25°C) for a maximum of 14 days. Do not store above 77°F (25°C). After removal from the refrigerator, DUPIXENT must be used within 14 days or discarded.

Do not expose the pre-filled syringe to heat or direct sunlight.

Do NOT freeze. Do NOT shake.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information and Instructions for Use).

Pregnancy Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to DUPIXENT during pregnancy. Encourage participation in the registry. [see Use in Specific Populations (8.1)].

Administration Instructions

Provide proper training to patients and/or caregivers on proper subcutaneous injection technique, including aseptic technique, and the preparation and administration of DUPIXENT prior to use. Advise patients to follow sharps disposal recommendations [see Instructions for Use].

Hypersensitivity

Advise patients to discontinue DUPIXENT and to seek immediate medical attention if they experience any symptoms of systemic hypersensitivity reactions [see Warnings and Precautions (5.1)].

Conjunctivitis and Keratitis

Advise patients to consult their healthcare provider if new onset or worsening eye symptoms develop [see Warnings and Precautions (5.2)].

Eosinophilic Conditions

Advise patients to notify their healthcare provider if they present with clinical features of eosinophilic pneumonia or vasculitis consistent with eosinophilic granulomatosis with polyangiitis [see Warnings and Precautions (5.3)].

Not for Acute Asthma Symptoms or Deteriorating Disease

Inform patients that DUPIXENT does not treat acute asthma symptoms or acute exacerbations. Inform patients to seek medical advice if their asthma remains uncontrolled or worsens after initiation of treatment with DUPIXENT [see Warnings and Precautions (5.4)].
Reduction in Corticosteroid Dosage

Inform patients to not discontinue systemic or inhaled corticosteroids except under the direct supervision of a physician. Inform patients that reduction in corticosteroid dose may be associated with systemic withdrawal symptoms and/or unmask conditions previously suppressed by systemic corticosteroid therapy [see Warnings and Precautions (5.5)].

Patients with Co-morbid Asthma

Advise patients with atopic dermatitis or CRSwNP who have co-morbid asthma not to adjust or stop their asthma treatment without talking to their physicians [see Warnings and Precautions (5.6)].