INDICATIONS AND USAGE

DUPIXENT is an interleukin-4 receptor alpha antagonist indicated:

- **Atopic Dermatitis**
- **Asthma**
- **Chronic Rhinosinusitis with Nasal Polyposis**
- **Eosinophilic Esophagitis**
- **Prurigo Nodularis**

**Dosage and Administration**

**Atopic Dermatitis**

Dosage in Adults (2.3):

Recommended dosage is an initial dose of 600 mg (two 300 mg injections), followed by 300 mg every other week (Q2W).

Dosage in Pediatric Patients 6 Months to 11 Years of Age (2.4):

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>Initial and Subsequent Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>15 to less than 30 kg</td>
<td>300 mg every 4 weeks (Q4W)</td>
</tr>
<tr>
<td>≥30 kg</td>
<td>200 mg every other week (Q2W)</td>
</tr>
</tbody>
</table>

**Asthma**

Dosage in Adult and Pediatric Patients 12 Years and Older (2.4):

<table>
<thead>
<tr>
<th>Initial Loading Dose</th>
<th>Subsequent Dosage*</th>
</tr>
</thead>
<tbody>
<tr>
<td>300 mg (two 300 mg injections)</td>
<td>200 mg every 2 weeks (Q2W)</td>
</tr>
<tr>
<td>600 mg (two 300 mg injections)</td>
<td>300 mg every 2 weeks (Q2W)</td>
</tr>
</tbody>
</table>

**Dosage in Pediatric Patients 6 to 11 Years of Age (2.4):**

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>Initial and Subsequent Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>15 to less than 30 kg</td>
<td>300 mg every 4 weeks (Q4W)</td>
</tr>
<tr>
<td>≥30 kg</td>
<td>200 mg every other week (Q2W)</td>
</tr>
</tbody>
</table>

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 2 which includes an initial loading dose. (2.3)

**Chronic Rhinosinusitis with Nasal Polyposis (2.5):**

Recommended dosage for adult patients is 300 mg given every other week (Q2W).

**Eosinophilic Esophagitis (2.6):**

Recommended dosage for adult and pediatric patients 12 years of age and older, weighing at least 40 kg, is 300 mg every other week (Q2W).

**Prurigo Nodularis (2.7):**

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

DOSE FORMS AND STRENGTHS

- Single-Dose Pre-Filled Syringe with Needle Shield (3):
  - Injection: 200 mg/1.14 mL
  - Injection: 300 mg/2 mL
- Single-Dose Pre-Filled Pen (3):
  - Injection: 200 mg/1.14 mL
  - Injection: 300 mg/2 mL

CONTRAINDICATIONS

Known hypersensitivity to dupilumab or any excipients in DUPIXENT. (4)

WARNINGS AND PRECAUTIONS

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

- Concomitant Use of Corticosteroids: Do not discontinue systemic, topical, or inhaled corticosteroids abruptly upon initiation of DUPIXENT. Decrease steroids gradually, if appropriate. (5.2)

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

- Arthralgia: 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. (5.7)

- Paraocular (Helminth) Infections: Treat pre-existing helminth infections before initiating DUPIXENT. If patients become infected while receiving DUPIXENT and do not respond to anti-helminth treatment, discontinue DUPIXENT until the infection resolves. (5.8)

- Vaccinations: Avoid use of live vaccines. (5.9)

ADVERSE REACTIONS

Most common adverse reactions are:

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

- Asthma (incidence ≥1%): injection site reactions, oropharyngeal pain, and eosinophilia. (6.1)

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

- Eosinophilic Esophagitis (incidence ≥2%): injection site reactions, upper respiratory tract infections, arthralgia, and herpes viral infections. (6.1)

- Prurigo Nodularis (incidence ≥2%): nasopharyngitis, conjunctivitis, herpes infection, dizziness, myalgia, and diarrhea. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Regeneron at 1-844-387-4936 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

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

Revised: 10/2023
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.
Table 2: Dosage of DUPLEXENT in Pediatric Patients 6 Years to 17 Years of Age with Atopic Dermatitis (continued)

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>Initial Loading Dose</th>
<th>Subsequent Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 to less than 60 kg</td>
<td>400 mg (two 200 mg injections)</td>
<td>200 mg every other week (Q2W)</td>
</tr>
<tr>
<td>60 kg or more</td>
<td>600 mg (two 300 mg injections)</td>
<td>300 mg every other week (Q2W)</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.

2.4 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 DUPLEXENT in Adult and Pediatric Patients 12 Years and Older with Asthma

<table>
<thead>
<tr>
<th>Initial Loading Dose</th>
<th>Subsequent Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>400 mg (two 200 mg injections)</td>
<td>200 mg every 2 weeks (Q2W)</td>
</tr>
<tr>
<td>or</td>
<td>600 mg (two 300 mg injections)</td>
</tr>
</tbody>
</table>

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 DUPLEXENT in Pediatric Patients 6 to 11 Years of Age with Asthma

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>Initial* and Subsequent Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>15 to less than 30 kg</td>
<td>300 mg every 4 weeks (Q4W)</td>
</tr>
<tr>
<td>≥30 kg</td>
<td>200 mg every other week (Q2W)</td>
</tr>
</tbody>
</table>

* 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 DUPLEXENT for adult patients is 300 mg given every other week.

2.6 Recommended Dosage for Eosinophilic Esophagitis

The recommended dosage of DUPLEXENT 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 DUPLEXENT for adult patients is an initial dose of 600 mg (two 300 mg injections) followed by 300 mg 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 DUPLEXENT from the refrigerator and allow DUPLEXENT to reach room temperature (45 minutes for the 300 mg/2 mL pre-filled syringe or pre-filled pen, and 30 minutes for the 200 mg/1.14 mL pre-filled syringe or pre-filled pen) without removing the needle cap. After removal from the refrigerator, DUPLEXENT must be used within 14 days or discarded.

Inspect DUPLEXENT visually for particulate matter and discoloration prior to administration. DUPLEXENT 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). DUPLEXENT 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

- 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 DUPLEXENT [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 DUPLEXENT 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 DUPLEXENT 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 DUPLEXENT and placebo [see Adverse Reactions (6.1)].

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

Conjunctivitis and keratitis adverse events have also been reported with DUPLEXENT 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 DUPLEXENT 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 DUPLEXENT 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 DUPLEXENT to treat acute bronchospasm or status asthmaticus. Patients should seek medical advice if their asthma remains uncontrolled or worsens after initiation of treatment with DUPLEXENT.

5.5 Risk Associated with Abrupt Reduction of Corticosteroid Dosage

Do not discontinue systemic, topical, or inhaled corticosteroids abruptly upon initiation of therapy with DUPLEXENT. 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 DUPLEXENT with some patients reporting gait disturbances or decreased mobility associated with joint symptoms; some cases resulted
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 during treatment 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 total, 48% of the subjects had asthma, 49% had allergic rhinitis, 37% had food allergy, and 27% had allergic conjunctivitis. In these 4 trials, 1472 patients with moderate-to-severe AD 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.

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 (continued)

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>DUPIXENT Monotherapya</th>
<th>DUPIXENT + TCSb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo 300 mg Q2W</td>
<td>N=529 n (%)</td>
<td>N=315 n (%)</td>
</tr>
<tr>
<td>Placebo 300 mg Q2W + TCS</td>
<td>N=517 n (%)</td>
<td>N=315 n (%)</td>
</tr>
</tbody>
</table>

Eye pruritus 3 (1) 1 (<1) 2 (2) 1 (<1)

Other herpes simplex virus infectionf 10 (2) 6 (1) 1 (1) 1 (<1)

Dry eye 1 (<1) 0 2 (2) 1 (<1)

f Pooled analysis of SOLO 1, SOLO 2, and AD-1021.

Safety through Week 52 (CHRONOS)

In the DUPIXENT with concomitant TCS trial (CHRONOS) 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.

Safety through 260 Weeks (AD-1225)

The long-term safety profile observed in this trial through 260 weeks was generally consistent with the safety profile of DUPIXENT observed in controlled studies.

Pediatric Subjects 12 to 17 Years of Age with Atopic Dermatitis

The safety of DUPIXENT was assessed in a trial of 250 pediatric subjects 12 to 17 years of age with moderate-to-severe AD (AD-1539). The safety profile of DUPIXENT in these subjects through Week 16 was similar to the safety profile seen in adults with AD.

The long-term safety of DUPIXENT was assessed in an open-label extension study in pediatric subjects 12 to 17 years of age with moderate-to-severe AD (AD-1434). The safety profile of DUPIXENT in subjects followed through Week 52 was similar to the safety profile observed at Week 16 in AD-1526. The long-term safety profile of DUPIXENT observed in pediatric subjects 12 to 17 years of age was consistent with that seen in adults with AD.

Pediatric Subjects 6 to 11 Years of Age with Atopic Dermatitis

The safety of DUPIXENT with concomitant TCS was assessed in a trial of 367 pediatric subjects 6 to 11 years of age with moderate-to-severe AD (AD-1652). The safety profile of DUPIXENT + TCS in these subjects through Week 16 was similar to the safety profile seen in adult and pediatric subjects 12 to 17 years of age with AD.

The long-term safety of DUPIXENT + TCS was assessed in an open-label extension study of 368 pediatric subjects 6 to 11 years of age with AD (AD-1434). Among subjects who entered the extension study, 110 (30%) had moderate AD and 72 (20%) had severe AD at the time of enrollment in AD-1434. The safety profile of DUPIXENT + TCS in subjects followed through Week 52 was similar to the safety profile observed through Week 16 in AD-1652. The long-term safety profile of DUPIXENT + TCS observed in pediatric subjects 6 to 11 years of age was consistent with that seen in adult and pediatric subjects 12 to 17 years of age with AD [see Use in Specific Populations (8.4)].

Pediatric Subjects 6 Months to 5 Years of Age with Atopic Dermatitis

The safety of DUPIXENT with concomitant TCS was assessed in a trial of 161 pediatric subjects 6 months to 5 years of age with moderate-to-severe AD (AD-1539). The safety profile of DUPIXENT + TCS in these subjects through Week 16 was similar to the safety profile from trials in adult and pediatric subjects 6 to 17 years of age with AD.

The long-term safety of DUPIXENT + TCS was assessed in an open-label extension study of 180 pediatric subjects 6 months to 5 years of age with AD (AD-1434). The majority of subjects were treated with DUPIXENT 300 mg every 4 weeks. The safety profile of DUPIXENT + TCS in subjects followed through Week 52 was similar to the safety profile observed through Week 16 in AD-1539. The long-term safety profile of DUPIXENT + TCS observed in pediatric subjects 6 months to 5 years of age was consistent with that seen in adults and pediatric subjects 6 to 17 years old with AD. In addition, hand-foot-and-mouth disease was reported in 9 (5%) pediatric subjects and skin papilloma was reported in 4 (2%) pediatric subjects treated with DUPIXENT + TCS. These cases did not lead to study drug discontinuation [see Use in Specific Populations (8.4)].

Asthma

Adults and Pediatric Subjects 12 Years of Age and Older with Asthma

A total of 2888 adult and pediatric subjects 12 to 17 years of age with moderate-to-severe asthma (AS) were evaluated in 3 randomized, placebo-controlled, multicenter trials of 24 to 52 weeks duration (DR12544, QUEST, and VENTURE). Of these, 2678 had a history of 1 or more exacerbations in the year prior to enrollment despite regular use of medium to high-dose inhaled corticosteroids plus an additional controller(s) (DR12544...
Injection site reactions were most common with the loading (initial) dose. A total of 210 subjects with oral corticosteroid-dependent asthma receiving high-dose inhaled corticosteroids plus up to two additional controllers were enrolled (VENTURE). The safety population (DRI12544 and QUEST) 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 DRI12544 and QUEST, 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 6 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 DRI12544 and QUEST.

### Table 6: Adverse Reactions Occurring in ≥1% of the DUPIXENT Groups in DRI12544 and QUEST and Greater than Placebo (6 Month Safety Pool)

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>DRI12544 and QUEST</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injection site reactions</td>
<td>111 (14%)</td>
<td>144 (18%)</td>
</tr>
<tr>
<td>Injection site reactions</td>
<td>13 (2%)</td>
<td>19 (2%)</td>
</tr>
<tr>
<td>Eosinophilia</td>
<td>17 (2%)</td>
<td>16 (2%)</td>
</tr>
</tbody>
</table>

a Injection site reactions cluster includes eczema, edema, pruritus, pain, and inflammation.

b Eosinophilia = blood eosinophils ≥0.000 cells/mL, or deemed by the investigator to be an adverse event. None met the criteria for serious eosinophilic conditions [see Warnings and Precautions (5.3)].

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.

**Pediatric Subjects 6 to 11 Years of Age with Asthma**

The safety of DUPIXENT was assessed in 405 pediatric subjects 6 to 11 years of age with moderate-to-severe asthma (VOYAGE). The safety profile of DUPIXENT in these subjects through Week 52 was similar to the safety profile from studies in adult and pediatric subjects 12 years of age and older with moderate-to-severe asthma with the addition of helminth infections. Helminth infections were reported in 2.2% (6 subjects) in the DUPIXENT group and 0.7% (1 subject) in the placebo group. The majority of cases were enterobiasis, reported in 1.8% (5 subjects) in the DUPIXENT group and none in the placebo group. There was one case of ascariasis in the DUPIXENT group. All helminth infection cases were mild to moderate and subjects recovered with anti-helminth treatment without DUPIXENT treatment discontinuation.

**Chronic Rhinosinusitis with Nasal Polyposis**

A total of 722 adult subjects with chronic rhinosinusitis with nasal polyposis (CRSwNP) were evaluated in 2 randomized, placebo-controlled, multicenter trials of 24 to 52 weeks duration (SINUS-24 and SINUS-52). 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 7 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 group in SINUS-24 and SINUS-52.

### Table 7: Adverse Reactions Occurring in ≥1% of the DUPIXENT Group in SINUS-24 and SINUS-52 and Greater than Placebo (24-Week Safety Pool)

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>SINUS-24 and SINUS-52</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injection site reactions</td>
<td>28 (6%)</td>
<td>12 (4%)</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>5 (1%)</td>
<td>0 (&lt;1%)</td>
</tr>
<tr>
<td>Eosinophilia</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.

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

**Eosinophilic Esophagitis**

A total of 239 adult and pediatric subjects 12 to 17 years of age, weighing at least 40 kg, and adults in Parts A and B were similar.

### Table 8: Adverse Reactions Occurring in ≥2% of Patients with EoE Treated with DUPIXENT in a Placebo Controlled Trial (Parts A and B; 24-Week Safety Pool)

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>DUPIXENT 300 mg QW</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injection site reactions</td>
<td>46 (38%)</td>
<td>39 (33%)</td>
</tr>
<tr>
<td>Upper respiratory tract infections</td>
<td>22 (18%)</td>
<td>12 (10%)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>2 (1%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Herpes viral infections</td>
<td>3 (2%)</td>
<td>1 (1%)</td>
</tr>
</tbody>
</table>

a Injection site reactions are composed of several terms including, but not limited to, injection site swelling, pain, and bruising.

b Upper respiratory tract infections are composed of several terms including, but not limited to, COVID-19, sinusitis, and upper respiratory tract infection.

c Herpes viral infections are composed of oral herpes and herpes simplex.

The safety profile of DUPIXENT in 72 pediatric subjects 12 to 17 years of age, weighing at least 40 kg, and adults in Parts A and B was similar.

**Prurigo Nodularis**

A total of 309 adult subjects with prurigo nodularis (PN) were evaluated in two 24-week randomized, double-blind, placebo-controlled, multicenter trials (PRIME and PRIME2). The safety pool included data from the 24-week treatment and 12-week follow-up periods from both trials. The proportion of subjects who discontinued treatment due to adverse events was 3% of the placebo group and 0% of the DUPIXENT 300 mg Q2W group. The safety population had a mean age of 49 years; 65% of subjects were female, 56% were White, 34% were Asian, and 6% were Black or African American. Subjects with co-morbid conditions included 43% of subjects with a history of atopy (defined as having a medical history of AD, allergic rhinitis/rhinoconjunctivitis, asthma, or food allergy), 8% of subjects with a history of hypothyroidism and 9% of subjects with a history of diabetes mellitus type 2. Table 9 summarizes the adverse reactions that occurred at a rate of at least 2% in subjects treated with DUPIXENT and at a higher rate than in their respective comparator group in PRIME and PRIME2.

### Table 9: Adverse Reactions Occurring in ≥2% of the DUPIXENT Group in PRIME and PRIME2 and Greater than Placebo

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>PRIME and PRIME2</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasopharyngitis</td>
<td>8 (5%)</td>
<td>3 (2%)</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>6 (4%)</td>
<td>2 (1%)</td>
</tr>
<tr>
<td>Herpes Infection</td>
<td>5 (3%)</td>
<td>0%</td>
</tr>
<tr>
<td>Dizziness</td>
<td>5 (3%)</td>
<td>2 (1%)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>5 (3%)</td>
<td>2 (1%)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4 (3%)</td>
<td>1 (1%)</td>
</tr>
</tbody>
</table>

a Nasopharyngitis includes pharyngitis.

b Conjunctivitis includes conjunctivitis and allergic conjunctivitis.

c Herpes infection includes oral herpes, genital herpes simplex, herpes zoster and ophthalmic herpes zoster.

d Dizziness includes dizziness postural, vertigo and vertigo positional.

e Myalgia includes musculoskeletal pain and musculoskeletal chest pain.

**Specific Adverse Reactions**

**Conjunctivitis and Keratitis**

In adult subjects with AD, conjunctivitis was reported in 10% (34 per 100 subject-years) in the 300 mg Q2W dose group and in 2% of the placebo group (8 per 100 subject-years) during the 16-week treatment period of the monotherapy trials (SOLO 1, SOLO 2, and AD-1021). During the 52-week treatment period of concomitant therapy AD trial (CHRONOS), conjunctivitis was reported in 16% of the DUPIXENT 300 mg Q2W + TCS.
Hypersensitivity Reactions

Hypersensitivity reactions were reported in <1% of DUXPENT-treated subjects. These included anaphylaxis, serum sickness or serum sickness-like reactions, generalized urticaria, rash, erythema nodosum, and erythema multiforme. 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. Additionally, 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.

Atopic Dermatitis

Approximately 6% of subjects with AD who received DUXPENT 300 mg Q2W for 52 weeks developed antibodies to DUXPENT; approximately 2% exhibited persistent ADA responses, and approximately 1% had neutralizing antibodies. Similar results were observed in pediatric subjects 6 months to 11 years of age with AD who received either DUXPENT 200 mg Q2W, 200 mg Q4W, or 300 mg Q4W.

Approximately 16% of pediatric subjects 12 to 17 years of age with AD who received DUXPENT 300 mg or 200 mg Q2W for 16 weeks developed antibodies to DUXPENT; approximately 6% exhibited persistent ADA responses, and approximately 5% had neutralizing antibodies.

Eosinophilic Esophagitis

Approximately 3% of subjects with EoE who received DUXPENT 300 mg Q2W for 52 weeks developed antibodies to DUXPENT; approximately 2% exhibited persistent ADA responses, and approximately 1% had neutralizing antibodies.

Chronic Rhinosinusitis with Nasal Polyps

Approximately 5% of subjects with asthma who received DUXPENT 300 mg Q2W for 52 weeks developed antibodies to DUXPENT; approximately 2% exhibited persistent ADA responses, and approximately 3% had neutralizing antibodies.

Skin and Subcutaneous Tissue Disorders

Facial skin reactions, including erythema, rash, scaling, edema, papules, pruritus, burning, and pain

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 DUXPENT during pregnancy. Healthcare providers and patients may call 1-877-311-8972 or go to https://clinicaltrialresults.org/ongoing-study/dupixent/treatment-effect-or-clinical-safety-information or other information about the registry.
The adverse event profile in pediatric subjects 12 to 17 years of age was generally similar to the adults [see Adverse Reactions (6.1)].

Pediatric Subjects 6 to 11 Years of Age:
A total of 408 pediatric subjects 6 to 11 years of age with moderate-to-severe asthma were enrolled in VOYAGE, which evaluated doses of 100 mg Q2W or 200 mg Q2W. In VOYAGE, in asthma exacerbations and lung function were demonstrated [see Clinical Studies (14.2)]. The effectiveness of DUPILUX 300 mg Q4W in subjects 6 to 11 years of age with body weight 15 to <30 kg was extrapolated from efficacy of 100 mg Q2W in VOYAGE with support from population pharmacokinetic analyses showing higher drug exposure levels with 300 mg Q4W [see Clinical Pharmacology (12.3)]. Subjects who completed the treatment period of the VOYAGE study could participate in the open-label extension study (LTS14424). Eighteen subjects (≥15 to <30 kg) out of 365 subjects were exposed to 300 mg Q4W in this study, and the safety profile in these eighteen subjects was similar to that seen in VOYAGE. Additional safety for DUPILUX 300 mg Q4W is based upon available safety information from the pediatric AD indication [see Adverse Reactions (6.1) and Clinical Pharmacology (12.3)].

Safety and effectiveness in pediatric patients younger than 6 years of age with asthma have not been established.

CRSwNP
Safety and effectiveness in pediatric patients younger than 18 years of age with CRSwNP have not been established.

EoE
The safety and effectiveness of DUPILUX for the treatment of EoE have been established in pediatric patients 12 years of age and older, weighing at least 40 kg. Use of DUPILUX in this population is supported by a adequate and well-controlled study in adults (Parts A and B) and included 72 pediatric patients 12 to 17 years of age, weighing at least 40 kg, and additional pharmacokinetic data. The safety and effectiveness in adults and pediatric patients were similar [see Adverse Reactions (6.1), Clinical Pharmacology (12.3) and Clinical Studies (14.3)].

The safety and effectiveness of DUPILUX for the treatment of EoE in pediatric patients less than 12 years of age and weighing less than 40 kg have not been established.

Prurigo Nodularis
Safety and effectiveness in pediatric patients younger than 18 years of age with PN have not been established.

5.7 Geriatric Use
Of the 1472 subjects with AD exposed to DUPILUX in a dose-ranging study and placebo-controlled trials, 67 subjects were 65 years or older. Clinical trials of DUPILUX in AD did not include sufficient numbers of subjects aged 65 years and over to determine whether they respond differently from younger subjects [see Clinical Pharmacology (12.3)].

Of the 1977 subjects with asthma exposed to DUPILUX, 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 DUPILUX, a total of 79 subjects were 65 years or older. Efficacy and safety in this age group were similar to the overall study population.

Clinical studies of DUPILUX in EoE did not include sufficient numbers of subjects aged 65 years and over to determine whether they respond differently from younger adult subjects.

Of the 152 subjects with PN exposed to DUPILUX, a total of 37 were 65 years or older and 12 of these subjects were 75 years or older. Clinical trials did not include a sufficient number of subjects 65 years of age and older to determine whether they respond differently from younger adult subjects.

10 OVERDOSAGE
There is no specific treatment for DUPILUX overdose. In the event of overdose, contact Poison Control (1-800-222-1222) for the latest recommendations and monitor the patient for any signs or symptoms of adverse reactions and institute appropriate symptomatic treatment immediately.

11 DESCRIPTION
Dulupriam, an interleukin-4 receptor alpha antagonist, is a human monoclonal antibody of IgG4 subtype that is to the IL-4Rα subunit and inhibits IL-4 and IL-13 signaling. Dulupriam has an approximate molecular weight of 147 kDa.

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

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

Each 300 mg pre-filled syringe or pre-filled pen delivers 300 mg dulupriam in 2 mL which also contains L-arginine hydrochloride (10.5 mg), L-histidine (6.2 mg), polysorbate 80 (4 mg), sodium acetate (2 mg), succrose (100 mg), and water for injection, pH 5.9.

Each 200 mg pre-filled syringe or pre-filled pen delivers 200 mg dulupriam in 1.14 mL which also contains L-arginine hydrochloride (12 mg), L-histidine (3.5 mg), polysorbate 80 (2.3 mg), sodium acetate (12.1 mg), sucrose (57 mg), and water for injection, pH 5.9.

12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
Dulupriam is a human monoclonal IgG4 antibody that inhibits interleukin-4 (IL-4) and interleukin-13 (IL-13) signaling by specifically binding to the IL-4/1 receptor and IL-13 receptor complexes. Dulupriam 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 atopy, AD, CRSwNP, EoE, and PN. Multiple cell types that express IL-4Rα (e.g., mast cells, eosinophils, basophils, langerhans cells, goblet cells) and inflammatory mediators (e.g., histamine, eicosanoids, leukotrienes, cytokines, chemokines) are involved in inflammation. Blocking IL-4R α 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 has been neither definitively established.

12.2 Pharmacodynamics

Consistent with inhibition of IL-4 and IL-13 signaling, dupilumab treatment decreased certain biomarkers of inflammation. In asthma subjects, fractional exhaled nitric oxide (FeNO) and circulating concentrations of eotaxin-3, total IgE, allergen specific IgE, TARC, and periostin was decreased relative to placebo. Reductions in these biomarkers were comparable for the 300 mg Q2W and 200 mg Q2W regimens. These markers were near maximal suppression after 2 weeks of treatment, except for IgE which declined more slowly. These effects were sustained throughout treatment. The median percent reduction from baseline in total IgE concentrations with dupilumab treatments was 52% at Week 24 and 70% at Week 52 (QUEST). For FeNO, the mean percent reduction from baseline at Week 2 was 35% and 24% in DR12544 and QUEST, respectively, and in the overall safety population, the mean FeNO level decreased to 20 ppb.

Antibody Response to Non-Live Vaccines During DUPIXENT Treatment

In a clinical study, adult subjects with AD were treated once weekly for 16 weeks with 300 mg of DUPLEXENT (twice the recommended dosing frequency). After 12 weeks of administration, subjects received a Tdap vaccine and a meningococcal polysaccharide vaccine. Antibody responses to tetanus toxoid and serogroup C meningococcal polysaccharide vaccine were decreased relative to placebo. Reductions in these biomarkers were consistent with inhibition of IL-4 and IL-13 signaling, dupilumab treatment decreased antibody responses to tetanus toxoid and serogroup C meningococcal polysaccharide were similar in DUPLEXENT-treated and placebo-treated subjects. Antibody responses to the other active components of both vaccines were not assessed. Antibody responses to other non-live vaccines were not assessed.

12.3 Pharmacokinetics

The pharmacokinetics of dupilumab is similar in subjects with AD, asthma, CRSwNP, EoE, and PN.

Absorption

Following an initial subcutaneous (SC) dose of 600 mg, 400 mg, or 300 mg, dupilumab reached peak mean ± SD concentrations (Cmax) of 70.1±24.1 mcg/mL, 41.8±12.4 mcg/mL, and 30.5±8.7 mcg/mL, respectively, by approximately 1 week post dose. Steady-state concentrations were achieved by Week 16 following the administration of 600 mg starting dose and 300 mg dose either weekly or Q2W, or 400 mg starting dose and 200 mg dose Q4W, or 300 mg Q2W without a loading dose. Across clinical trials, the mean ± SD steady-state trough concentrations ranged from 90±33.5 mcg/mL to 80±25.3 mcg/mL for 300 mg administered Q2W, from 173±75.9 mcg/mL to 195±71.7 mcg/mL for 300 mg administered weekly, and from 29.2±18.7 to 36.5±22.2 mcg/mL for 200 mg administered Q2W.

The bioavailability of dupilumab following a SC dose is similar between AD, asthma, CRSwNP, EoE, and PN subjects, ranging between 61% and 64%.

Distribution

The estimated total volume of distribution was approximately 4.8±1.3 L.

Elimination

The metabolic pathway of dupilumab has not been characterized. As a human monoclonal IgG4 antibody, dupilumab is expected to be degraded into small peptides and amino acids via catabolic pathways in the same manner as endogenous IgG. Following the administration of dupilumab, serum concentrations declined by at least 3.3-fold for the total IgG fraction and 3.9-fold for the IgG1 fraction and 2.5-fold for the IgG4 fraction. The IgG4 antibody, dupilumab is expected to be degraded into small peptides and amino acids after the last steady-state trough concentration of dupilumab was 54.5±27.0 mcg/mL.

Following an initial subcutaneous (SC) dose of 600 mg, 400 mg, or 300 mg, dupilumab reached peak mean ± SD concentrations (Cmax) of 70.1±24.1 mcg/mL, 41.8±12.4 mcg/mL, and 30.5±8.7 mcg/mL, respectively, by approximately 1 week post dose. Steady-state concentrations were achieved by Week 16 following the administration of 600 mg starting dose and 300 mg dose either weekly or Q2W, or 400 mg starting dose and 200 mg dose Q4W, or 300 mg Q2W without a loading dose. Across clinical trials, the mean ± SD steady-state trough concentrations ranged from 90±33.5 mcg/mL to 80±25.3 mcg/mL for 300 mg administered Q2W, from 173±75.9 mcg/mL to 195±71.7 mcg/mL for 300 mg administered weekly, and from 29.2±18.7 to 36.5±22.2 mcg/mL for 200 mg administered Q2W.

The bioavailability of dupilumab following a SC dose is similar between AD, asthma, CRSwNP, EoE, and PN subjects, ranging between 61% and 64%.

Dose Linearity

Dupilumab exhibited nonlinear target-mediated pharmacokinetics with exposures increasing in a greater than dose-proportional manner. The systemic exposure increased by 30-fold when the dose increased 8-fold following a single dose of dupilumab from 75 mg to 600 mg (i.e., 0.25-times to the recommended dose).

Weight

Dupilumab trough concentrations were lower in subjects with higher body weight.

Age

Based on population pharmacokinetic analysis, age did not affect dupilumab clearance in adults and in pediatric subjects 6 to 17 years of age. In pediatric subjects 6 months to 5 years of age, clearance increased with age.

Immunogenicity

Development of antibodies to dupilumab was associated with lower serum dupilumab concentrations.

Drug Interaction Studies

An effect of dupilumab on the PK of co-administered medications is not expected. Based on the population analysis, commonly co-administered medications had no effect on DUPLEXENT pharmacokinetics in subjects with moderate-to-severe asthma.

Cytochrome P450 Substrates

The effects of dupilumab on the pharmacokinetics of midazolam (metabolized by CYP3A4), warfarin (metabolized by CYP2C9), omeprazole (metabolized by CYP2C19), metoprolol (metabolized by CYP2D6), and caffeine (metabolized by CYP1A2) were evaluated in a study with 12-13 evaluable subjects with AD (a SC loading dose of 600 mg of dupilumab and 0.48 mg of metoprolol 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-4R α 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 (SOLO 1 (NCT02277743), SOLO 2 (NCT02277769), and CHRONOS (NCT02260986)) enrolled a total of 2119 adult subjects 18 years of age and older with moderate-to-severe 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 DUPLEXENT group received subcutaneous injections of DUPLEXENT 600 mg at Week 0, followed by 300 mg every other week (Q2W). In the monotherapy trials (SOLO 1 and SOLO 2), subjects received DUPLEXENT or placebo for 16 weeks.

In the concomitant therapy trial (CHRONOS), subjects received DUPLEXENT 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 the proportion of subjects with an IGA 0 (clear) or 1 (almost clear) and at least a 2-point improvement. Other endpoints included the proportion of subjects with EASI-75 (improve of at least 75% in EASI score from baseline), and reduction in itch as defined by at least a 4-point improvement in the Peak Pruritus NRS from baseline to Week 16.

Clinical Response at Week 16 (SOLO 1, SOLO 2, and CHRONOS)

The results of the DUPLEXENT monotherapy trials (SOLO 1 and SOLO 2) and the DUPLEXENT with concomitant TCS trial (CHRONOS) are presented in Table 10.
In CHRONOS, of the 421 randomized and treated subjects, 68 subjects (16%) had not been on study for 52 weeks at the time of data analysis. In CHRONOS, of the 421 subjects, 353 had been on study for 52 weeks at the time of data analysis. Of these 353 subjects, responders at Week 16 who later responded to treatment (e.g., 24% of DUPIXENT responders at Week 16 remained responders at Week 52). Results of supportive analyses of the 353 subjects in the DUPIXENT with concomitant TCS trial (CHRONOS) are presented in Table 11.

Table 11: Efficacy Results (IGA 0 or 1) of DUPIXENT with Concomitant TCS at Week 16 and 52 in Adult Subjects 18 Years of Age and Older with Moderate-to-Severe AD

<table>
<thead>
<tr>
<th>Subjects</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>Responder at Week 16 and 52</td>
<td>22%</td>
<td>7%</td>
</tr>
<tr>
<td>Non-responder at Week 16 and Responder at Week 52</td>
<td>13%</td>
<td>6%</td>
</tr>
<tr>
<td>Overall Responder Rate at Week 52</td>
<td>36%</td>
<td>13%</td>
</tr>
</tbody>
</table>

In SOLO 1, SOLO 2, and CHRONOS, a third randomized treatment arm of DUPIXENT monotherapy dose regimens for maintaining treatment response. The study included subjects randomized to continue with DUPIXENT 300 mg QW (62 subjects) or switch to placebo (31 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.

Pediatric Subjects 12 to 17 Years of Age with Atopic Dermatitis

The efficacy of DUPIXENT monotherapy in pediatric subjects 12 to 17 years of age was evaluated in a multicenter, randomized, double-blind, placebo-controlled trial (AD-1526; NCT03054428) in 251 pediatric subjects 12 to 17 years of age, with moderate-to-severe AD defined by an IGA score ≥3 (scale of 0 to 4), 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 <50 kg received an initial dose of 400 mg at Week 0, followed by 200 mg Q2W for 16 weeks. Subjects with baseline weight of ≥50 kg received an initial dose of 600 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 AD-1526, 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. At baseline, 49% 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 co-morbid allergic condition; 86% 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 evaluated 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 AD-1526 are presented in Table 12.

Table 12: Efficacy Results of DUPIXENT in AD-1526 at Week 16 (FAS)* in Pediatric Subjects 12 to 17 Years of Age with Moderate-to-Severe AD

<table>
<thead>
<tr>
<th>Subjects</th>
<th>DUPIXENT* 200 mg (&lt;60 kg) or 300 mg (&lt;80 kg) Q2W N=82*</th>
<th>Placebo N=85*</th>
</tr>
</thead>
<tbody>
<tr>
<td>IGA 0 or 1</td>
<td>24%</td>
<td>2%</td>
</tr>
<tr>
<td>EASI-75</td>
<td>42%</td>
<td>8%</td>
</tr>
<tr>
<td>EASI-90</td>
<td>23%</td>
<td>2%</td>
</tr>
<tr>
<td>Peak Pruritus NRS (&gt;4-point improvement)**</td>
<td>37%</td>
<td>5%</td>
</tr>
</tbody>
</table>

* Full Analysis Set (FAS) includes all subjects randomized.
** 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.
* Subjects who received rescue treatment or with missing data were considered as non-responders.

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.

In CHRONOS, of the 421 randomized treated subjects, 68 subjects (16%) had not been on study for 52 weeks at the time of data analysis. In CHRONOS, of the 421 randomized treated subjects, 88 subjects (16%) had not been on study for 52 weeks at the time of data analysis. Subjects who received rescue treatment or with missing data were considered non-responders.
Pediatric Subjects 6 to 11 Years of Age with Atopic Dermatitis

The efficacy and safety of DUXIPENT use concomitantly with TCS in pediatric subjects was evaluated in a multicenter, randomized, double-blind, placebo-controlled trial (AD-1652; NCT03345914) in 367 subjects 6 to 11 years of age, with AD defined by an IGA score of ≥4 (scale of 0 to 4), an EASI score ≥21 (scale of 0 to 72), and a minimum BSA involvement of ≥15%. Eligible subjects enrolled into this trial had previous inadequate response to topical medication. Enrollment was stratified by baseline weight (<30 kg; ≥30 kg).

Subjects in the DUXIPENT Q4W + TCS group received an initial dose of 600 mg on Day 1, followed by 300 mg Q4W from Week 4 to Week 12, regardless of weight. Subjects in the DUXIPENT Q2W + TCS group with baseline weight of <30 kg received an initial dose of 200 mg on Day 1, followed by 100 mg Q2W from Week 2 to Week 14, and subjects with baseline weight of ≥30 kg received an initial dose of 400 mg on Day 1, followed by 200 mg Q2W from Week 2 to Week 14. Subjects were permitted to receive rescue treatment at the discretion of the investigator. Subjects who received rescue treatment were considered non-responders.

In AD-1652, the mean age was 8.5 years, the median weight was 29.8 kg, 50% of subjects were female, 69% were White, 17% were Black, and 8% were Asian. At baseline, the mean BSA involvement was 58%, and 17% had received prior systemic non-steroidal immunosuppressants. Also, at baseline the mean EASI score was 37.9, and the weekly average of daily worst itch score was 7.8 on a scale of 0-10. Overall, 92% of subjects had at least one co-morbid allergic condition; 64% had food allergies, 63% had other allergies, 60% had allergic rhinitis, and 47% had asthma.

The primary endpoint was the proportion of subjects with an IGA 0 (clear) or 1 (almost clear) at Week 16. Other evaluated 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 and Worst Scratch/Itch NRS (≥4-point improvement).

Table 13 presents the results by baseline weight strata for the approved dose regimens.

Table 13: Efficacy Results of DUXIPENT with Concomitant TCS in AD-1652 at Week 16 (FAS)a in Pediatric Subjects 6 to 11 Years of Age with AD

<table>
<thead>
<tr>
<th></th>
<th>DUXIPENT 300 mg Q4W + TCS</th>
<th>Placebo + TCS</th>
<th>DUXIPENT 200 mg Q2W + TCS</th>
<th>Placebo + TCS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(N=61)</td>
<td>(N=61)</td>
<td>(N=59)</td>
<td>(N=62)</td>
</tr>
<tr>
<td>&lt;30 kg</td>
<td>&lt;30 kg</td>
<td>≥30 kg</td>
<td>≥30 kg</td>
<td></td>
</tr>
<tr>
<td>IGA 0 or 1abc</td>
<td>30%</td>
<td>13%</td>
<td>39%</td>
<td>10%</td>
</tr>
<tr>
<td>EASI-75c</td>
<td>75%</td>
<td>28%</td>
<td>75%</td>
<td>26%</td>
</tr>
<tr>
<td>EASI-90c</td>
<td>46%</td>
<td>7%</td>
<td>36%</td>
<td>8%</td>
</tr>
<tr>
<td>Peak Pruritus NRS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥4-point improvement</td>
<td>54%</td>
<td>12%</td>
<td>61%</td>
<td>13%</td>
</tr>
</tbody>
</table>

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.

c At Day 1, subjects received 200 mg (baseline weight <30 kg) or 400 mg (baseline weight ≥30 kg) of DUXIPENT.

A greater proportion of subjects randomized to DUXIPENT + TCS achieved an improvement in the Peak Pruritus NRS compared to placebo + TCS (defined as ≥4-point improvement at Week 16). See Figure 3.

14.2. Asthma

The asthma development program for patients aged 12 years and older included three randomized, double-blind, placebo-controlled, parallel-group, multicenter trials (DR12544 (NCT01854047), QUEST (NCT02414854), and VENTURE (NCT02528214)) of 24 to...
Table 15: Demographics and Baseline Characteristics of Asthma Trials (continued)

Table 16: Rate of Severe Exacerbations in DRI12544 and QUEST

Exacerbations

DRI12544 and QUEST 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/mL in DRI12544 and the overall population in QUEST), subjects receiving either DUXIPENT 200 mg or 300 mg Q2W had significant reductions in the rate of asthma exacerbations compared to placebo. In the overall population in QUEST, the rate of severe exacerbations was 0.46 and 0.52 for DUXIPENT 200 mg Q2W and 300 mg Q2W, respectively, compared to matched placebo rates of 0.67 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 DUXIPENT 200 mg Q2W and 300 mg Q2W, respectively. Results in subjects with baseline blood eosinophil counts ≥300 cells/mL in DRI12544 and QUEST are shown in Table 16.

Response rates by baseline blood eosinophils and baseline FeNO for QUEST are shown for the overall population in Figure 4 and Figure 5, respectively. Elevation of FeNO can be a marker of the eosinophilic asthma phenotype when supported by clinical data. Pre-specified subgroup analyses of DRI12544 and QUEST demonstrated that there were greater reductions in severe exacerbations in subjects with higher baseline blood eosinophil levels (≥150 cells/mL) or FeNO (≥25 ppb). In QUEST, reductions in exacerbations were significant in the subgroup of subjects with baseline blood eosinophils ≥150 cells/mL. In subjects with baseline blood eosinophil count <150 cells/mL and FeNO <25 ppb, similar severe exacerbation rates were observed between DUXIPENT and placebo.

In QUEST, the estimated rate ratio of exacerbations leading to hospitalizations and/or emergency room visits versus placebo was 0.53 (95% CI: 0.28, 1.03) and 0.74 (95% CI: 0.32, 1.70) with DUXIPENT 200 mg or 300 mg Q2W, respectively.
Mean changes in FEV1 and placebo. Results in subjects with baseline blood eosinophil counts ≥300 cells/mL (QUEST) were observed at Week 12 for DRI12544 compared to placebo in QUEST (Figure 6).

The time to first exacerbation was longer for the subjects receiving DUPIXENT compared to placebo in QUEST (Figure 6).

Figure 6: Kaplan Meier Incidence Curve for Time to First Severe Exacerbation in Subjects with Moderate-to-Severe Asthma with Baseline Blood Eosinophils ≥300 cells/mL (QUEST)*

<table>
<thead>
<tr>
<th>Treatment</th>
<th>N</th>
<th>LS Mean Change from baseline L (%)</th>
<th>LS Mean Difference vs. placebo (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DRI12544</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DUPIXENT 200 mg Q2W</td>
<td>65</td>
<td>0.43 (25.9)</td>
<td>0.26 (0.11, 0.40)</td>
</tr>
<tr>
<td>DUPIXENT 300 mg Q2W</td>
<td>64</td>
<td>0.39 (25.8)</td>
<td>0.21 (0.06, 0.36)</td>
</tr>
<tr>
<td>Placebo</td>
<td>68</td>
<td>0.18 (10.2)</td>
<td></td>
</tr>
<tr>
<td>QUEST</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DUPIXENT 200 mg Q2W</td>
<td>264</td>
<td>0.43 (29.0)</td>
<td>0.21 (0.13, 0.29)</td>
</tr>
<tr>
<td>Placebo</td>
<td>148</td>
<td>0.21 (15.6)</td>
<td></td>
</tr>
<tr>
<td>DUPIXENT 300 mg Q2W</td>
<td>277</td>
<td>0.47 (32.5)</td>
<td>0.24 (0.16, 0.32)</td>
</tr>
<tr>
<td>Placebo</td>
<td>142</td>
<td>0.22 (14.4)</td>
<td></td>
</tr>
</tbody>
</table>

Additional Secondary Endpoints
ACQ-5 and AQLQ(S) were assessed in QUEST 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 1.61; 95% CI: 1.17, 2.21) and 62% vs 57% placebo (odds ratio 1.33; 95% CI: 0.98, 1.81), respectively.

Oral Corticosteroid Reduction (VENTURE)
VENTURE 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 DUPIXENT achieved greater reductions in daily maintenance oral corticosteroid dose, while maintaining asthma control. The mean percent reduction in daily OCS dose from baseline was 70% (median 100%) in subjects receiving DUPIXENT (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 52% (80%) subjects receiving DUPIXENT compared to 27% (63%) in those receiving placebo. The proportion of subjects with a mean final dose less than 5 mg at Week 24 was 72% for DUPIXENT and 37% for placebo (odds ratio 4.48 95% CI: 2.39, 8.63).
8.39). A total of 54 (52%) subjects receiving DUXPIENT 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 DUXPIENT compared to those receiving placebo (annualized rate 0.65 and 1.60 for the DUXPIENT and placebo group, respectively; rate ratio 0.41 [95% CI 0.28, 0.63]) and improvement in pre-bronchodilator FEV₁, from baseline to Week 24 was greater in subjects receiving DUXPIENT compared to those receiving placebo (LS mean difference for DUXPIENT 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 ACO-5 and AQLQ(S) were also assessed in VENTURE and showed improvements similar to those in QUEST.

Pediatric Subjects 6 to 11 Years of Age with Asthma

The efficacy and safety of DUXPIENT in pediatric subjects was evaluated in a 52-week multicenter, randomized, double-blind, placebo-controlled study (VOYAGE; NCT02949959) in 408 subjects 6 to 11 years of age, with moderate-to-severe asthma on a medium or high-dose ICS and a second controller medication or high-dose ICS alone. Subjects were required to have a history of 1 or more asthma exacerbation(s) 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 were randomized to DUXPIENT (N=273) or matching placebo (N=155) every other week based on weight body <30 kg (100 mg Q2W) or ≥30 kg (200 mg Q2W). The effectiveness of DUXPIENT 300 mg Q4W was extrapolated from efficacy of 100 mg Q2W in VOYAGE with support from population pharmacokinetic analyses showing higher drug exposure levels with 300 mg Q4W [see Pediatric Use (8.4) and Pharmacokinetics (12.3)].

The primary endpoint was the annualized rate of severe asthma exacerbation events during the 52-week placebo-controlled period. Severe asthma exacerbations were 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. The key secondary endpoint was the change from baseline in pre-bronchodilator FEV₁, percent predicted at Week 12. Additional secondary endpoints included mean change from baseline and responder rates in the ACO-7-IA (Asthma Control Questionnaire-7-Interviewer Administered) and PAQLQ(S)-IA (Pediatric Asthma Quality of Life Questionnaire with Standardized Activities Interviewer Administered) scores. Improvements were also observed for ACQ-7-IA and PAQLQ(S)-IA at Week 24 and were sustained at Week 52. Greater responder rates were observed for ACO-7-IA and PAQLQ(S)-IA compared to placebo at Week 24. The responder rate was defined as an improvement in score of 0.5 or more (scale range 0-6 for ACO-7-IA and 1-7 for PAQLQ(S)-IA). In the subgroup of subjects with baseline blood eosinophil count ≥300 cells/mL, DUXPIENT led to a higher proportion of subjects with a response in ACO-7-IA (80.6% versus 64.3% for placebo) with an OR of 2.79 (95% CI: 1.43, 5.44), and in PAQLQ(S)-IA (72.8% versus 63.0% for placebo) with an OR of 1.84 (95% CI: 0.92, 3.65) at Week 24.

14.3 Chronic Rhinosinusitis with Nasal Polyposis

The chronic rhinosinusitis with nasal polyps (CRS with NP) development program included two randomized, double-blind, parallel-group, multicenter, placebo-controlled studies (SINUS-24 [NCT02912468] and SINUS-52 [NCT02898543]) in 725 adult subjects 16 years of age and older on background intranasal corticosteroids (IICS). These studies included subjects with CRS with NP 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. Subjects with chronic rhinosinusitis without nasal polyps were not included in these trials. Rescue with systemic corticosteroids or surgery was allowed during the studies at the investigator’s discretion. In SINUS-24, a total of 276 subjects were randomized to receive either 300 mg DUXPIENT (N=143) or placebo (N=133) every other week for 24 weeks. In SINUS-52, 448 subjects were randomized to receive either 300 mg DUXPIENT (N=150) every other week for 52 weeks, 300 mg DUXPIENT (N=145) every other week until Week 24 followed by 300 mg DUXPIENT every 4 weeks until Week 52, or placebo (N=153). All subjects had evidence of sinus 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 endoscopic nasal polyps score (NPS, 0-8 scale) as graded by certified blinded readers, and change from baseline to Week 24 in nasal congestion obstruction score averaged over 28 days (NC; 0-3 scale), as determined by subjects using a daily diary. For NPS, polyps on each side of the nose were graded on a categorical scale (0=no polyps; 1=small polyps in the middle meatus not reaching below the inferior border of the middle turbinate; 2=polyps reaching below the lower border of the middle turbinate; 3=large polyps reaching the lower border of the inferior turbinate or polyps 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 rated daily by the subjects on a 0 to 3 categorical severity scale (0=no symptoms; 1=mild symptoms; 2=moderate symptoms; 3=severe symptoms).

The demographics and baseline characteristics for VOYAGE are provided in Table 18 below.

Table 18: Demographics and Baseline Characteristics for VOYAGE

<table>
<thead>
<tr>
<th>Parameter</th>
<th>VOYAGE (N=408)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years) (SD)</td>
<td>9 (2)</td>
<td></td>
</tr>
<tr>
<td>% Female</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>% White</td>
<td>88</td>
<td></td>
</tr>
<tr>
<td>Mean body weight (kg)</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>Mean exacerbations in previous year (± SD)</td>
<td>2.4 (2.2)</td>
<td></td>
</tr>
<tr>
<td>High dose ICS use (%)</td>
<td>44</td>
<td></td>
</tr>
<tr>
<td>Pre-dose FEV₁ (L) at baseline (± SD)</td>
<td>1.48 (0.41)</td>
<td></td>
</tr>
<tr>
<td>Mean percent predicted FEV₁ (%) (±SD)</td>
<td>78 (15)</td>
<td></td>
</tr>
<tr>
<td>Mean % Reversibility (± SD)</td>
<td>20 (21)</td>
<td></td>
</tr>
<tr>
<td>Atopic Medical History % Overall (AD %, AR %)</td>
<td>92 (36, 82)</td>
<td></td>
</tr>
<tr>
<td>Mean FeNO ppb (± SD)</td>
<td>28 (24)</td>
<td></td>
</tr>
<tr>
<td>% subjects with FeNO ppb ≥20</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>Median total IgE IU/mL (±SD)</td>
<td>792 (1093)</td>
<td></td>
</tr>
<tr>
<td>Mean baseline Eosinophil count (± SD) cells/mL</td>
<td>502 (395)</td>
<td></td>
</tr>
</tbody>
</table>

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

DUXPIENT significantly reduced the annualized rate of severe asthma exacerbation events during the 52-week treatment period compared to placebo in populations with an eosinophilic phenotype or defined by elevated blood eosinophilophils and/or the population with elevated FeNO. Subgroup analyses for results of DUXPIENT treatment based upon either baseline eosinophil level or baseline FeNO level were similar to the pediatric (12 to 17 years of age) asthma population above. In subjects with baseline blood eosinophil count <150 cells/mL and FeNO <30 ppb, similar severe asthma exacerbation rates were observed between DUXPIENT and placebo.

Significant improvements in percent predicted pre-bronchodilator FEV₁ were observed at Week 12. Significant improvements in percent predicted FEV₁ were observed as early as Week 2 and were maintained through Week 52 in VOYAGE (Figure 10).

The efficacy results for VOYAGE are presented in Table 19.

Table 19: Efficacy Results of DUXPIENT in VOYAGE

<table>
<thead>
<tr>
<th>Treatment</th>
<th>EOS ≥300 cells/mL*</th>
<th>N</th>
<th>Rate (95% CI)</th>
<th>Rate Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DUXPIENT</td>
<td>175</td>
<td>0.24 (0.16, 0.35)</td>
<td>0.35 (0.22, 0.56)</td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>84</td>
<td>0.67 (0.47, 0.95)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*This reflects the prespecified primary analysis population for VOYAGE in the United States.

Figure 10: Mean Change from Baseline in Percent Predicted pre-bronchodilator FEV₁ (L) Over Time in Pediatric Subjects 6 to 11 Years of Age in VOYAGE (Baseline Blood Eosinophilophils ≥300 cells/mL)

Improvements were also observed for ACQ-7-IA and PAQLQ(S)-IA at Week 24 and were sustained at Week 52. Greater responder rates were observed for ACQ-7-IA and PAQLQ(S)-IA compared to placebo at Week 24. The responder rate was defined as an improvement in score of 0.5 or more (scale range 0-6 for ACQ-7-IA and 1-7 for PAQLQ(S)-IA). In the subgroup of subjects with baseline blood eosinophil count ≥300 cells/mL, DUXPIENT led to a higher proportion of subjects with a response in ACQ-7-IA (80.6% versus 64.3% for placebo) with an OR of 2.79 (95% CI: 1.43, 5.44), and in PAQLQ(S)-IA (72.8% versus 63.0% for placebo) with an OR of 1.84 (95% CI: 0.92, 3.65) at Week 24.
In both studies, key secondary end-points at Week 24 included change from baseline in: LMK sinus CT scan score, daily loss of smell, and 22-item sino-nasal outcome test (SNOT-22). The LMK sinus CT scan score evaluated the opacification of each sinus using a 0 to 2 scale (0=normal; 1=mild opacification; 2=moderate opacification; 3=severe opacification). SNOT-22 includes 22 items assessing symptoms and symptom impact associated with CRSwNP with each item scored from 0 (no problem) to 5 (problem as bad as it can be) with a global score ranging from 0 to 110. SNOT-22 was scored every 2 weeks. In the post-treatment period when subjects were off DUPIXENT, the treatment effect diminished over time (see Figure 12). Similar results were seen in SINUS-24 at Week 24. In the post-treatment period when subjects were off DUPIXENT, the treatment effect diminished over time (see Figure 12). The demographics and baseline characteristics of these 2 trials are provided in Table 20 below.

### Table 20: Demographics and Baseline Characteristics of CRSwNP Trials

<table>
<thead>
<tr>
<th>Parameter</th>
<th>SINUS-24 (N=276)</th>
<th>SINUS-52 (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>Subjects with ≥1 prior surgery (%)</td>
<td>72</td>
<td>58</td>
</tr>
<tr>
<td>Subjects with systemic corticosteroid use in the previous 2 years (%)</td>
<td>65</td>
<td>80</td>
</tr>
<tr>
<td>Mean Bilateral 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>
</tbody>
</table>

### Table 21: Results of the Primary Endpoints in CRSwNP Trials

<table>
<thead>
<tr>
<th>Primary Endpoints at Week 24</th>
<th>Placebo (n=133)</th>
<th>DUPIXENT 300 mg Q2W (n=143)</th>
<th>LS mean difference vs. Placebo (95% CI)</th>
<th>Placebo (n=153)</th>
<th>DUPIXENT 300 mg Q2W (n=295)</th>
<th>LS mean difference vs. Placebo (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scores</td>
<td>Baseline mean</td>
<td>LS mean change</td>
<td>Baseline mean</td>
<td>LS mean change</td>
<td>Baseline mean</td>
<td>LS mean change</td>
</tr>
<tr>
<td>NPS</td>
<td>5.86</td>
<td>0.17</td>
<td>5.64</td>
<td>-1.89</td>
<td>-2.06 (-2.43, -1.69)</td>
<td>5.96</td>
</tr>
<tr>
<td>NC</td>
<td>2.45</td>
<td>-0.45</td>
<td>2.26</td>
<td>-1.34</td>
<td>-0.89 (-1.07, -0.71)</td>
<td>2.38</td>
</tr>
</tbody>
</table>

A reduction in score indicates improvement.

NPS = nasal polyps score; NC = nasal congestion/obstruction

Statistically significant efficacy was observed in SINUS-52 with regard to improvement in bilateral endoscopic NPS score at week 24 and week 52 (see Figure 11).

### Figure 11: LS Mean Change from Baseline in Bilateral Nasal Polyps Score (NPS) up to Week 52 in Subjects 18 Years of Age and Older with CRSwNP (SINUS-52 - ITT Population)

![Figure 11: LS Mean Change from Baseline in Bilateral Nasal Polyps Score (NPS) up to Week 52 in Subjects 18 Years of Age and Older with CRSwNP (SINUS-52 - ITT Population)](image)

Similar results were seen in SINUS-24 at Week 24. In the post-treatment period when subjects were off DUPIXENT, the treatment effect diminished over time (see Figure 12).

### Table 20: Demographics and Baseline Characteristics of CRSwNP Trials (continued)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>SINUS-24 (N=276)</th>
<th>SINUS-52 (N=448)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean 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>Subjects with ≥1 prior surgery (%)</td>
<td>72</td>
<td>58</td>
</tr>
<tr>
<td>Subjects with systemic corticosteroid use in the previous 2 years (%)</td>
<td>65</td>
<td>80</td>
</tr>
<tr>
<td>Mean Bilateral 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>
</tbody>
</table>

### Figure 12: LS Mean Change from Baseline in Bilateral Nasal Polyps Score (NPS) up to Week 48 in Subjects 18 Years of Age and Older with CRSwNP (SINUS-24 - 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 SINUS-24 and -0.37 (95% CI -0.46, -0.27) in SINUS-52. A significant decrease 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 -8.35, -6.53) in SINUS-24 and -5.13 (95% CI -5.86, -4.46) in SINUS-52. At Week 52, in SINUS-52 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 SINUS-24 and -0.98 (95% CI -1.15, -0.81) in SINUS-52. At Week
52, the LS mean difference for loss of smell in the DUXIPENT 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.

Dulaglutide 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 DUXIPENT group versus placebo was -21.12 (95% CI: -25.17, -17.06) in SINOUS-24 and -17.36 (95% CI: -20.87, -13.85) in SINOUS-52. At Week 52, the LS mean difference in the DUXIPENT 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 DUXIPENT 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 13). 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 was reduced by 75% (RR of 0.25; 95% CI: 0.17, 0.37). The proportion of subjects who required surgery was reduced by 83% (HR of 0.17; 95% CI: 0.07, 0.46).

Figure 13: Kaplan Meier Curve for Time to First Systemic Corticosteroid Use and/or Sino-Nasal Surgery During Treatment Period in Subjects 18 Years of Age and Older with CRSwNP (SINOUS-24 and SINOUS-52 - ITT Population)

The coprimary efficacy endpoints in Parts A and B were the (1) proportion of subjects achieving histological remission defined as peak esophageal intraepithelial eosinophil count ≤6 eos/hpf at Week 24; and (2) the absolute change in the subject-reported DSQ score from baseline to Week 24.

### Efficacy Results of DUXIPENT at Week 24 in Subjects 12 Years of Age and Older with EoE (Parts A and B)

<table>
<thead>
<tr>
<th>Co-primary Endpoints</th>
<th>Part A</th>
<th>Part B</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Proportion of subjects achieving histological remission</strong> (peak esophageal intraepithelial eosinophil count ≤6 eos/hpf), n (%)</td>
<td>DUXIPENT 300 mg QW&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Placebo&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>N = 42</td>
<td>N = 39</td>
<td>N = 80</td>
</tr>
<tr>
<td>25 (59.5)</td>
<td>2 (5.1)</td>
<td>57.0 (40.9, 73.1)</td>
</tr>
<tr>
<td>Absolute change from baseline in DSQ score (0-84&lt;sup&gt;b&lt;/sup&gt;), LS mean (SE)</td>
<td>-21.9 (2.5)</td>
<td>-9.6 (2.8)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Total biopsy DSQ scores range from 0 to 84; higher scores indicate greater frequency and severity of dysphagia

<sup>b</sup> For histological remission, the difference in percentages is estimated using the Cochran Mantel Haenszel method, adjusting for randomization stratification factors. For absolute change in DSQ score, the LS mean changes, standard errors, and differences are estimated using an ANCOVA model with treatment group, randomization stratification factors, and baseline measurement as covariates.

In Parts A and B, a greater proportion of subjects randomized to DUXIPENT achieved histological remission (peak esophageal intraepithelial eosinophil count ≤6 eos/hpf) compared to placebo. Treatment with DUXIPENT also resulted in a significant improvement in LS mean change in DSQ score compared to placebo at Week 24. The results of the anchor-based analyses that incorporated the subjects’ perspectives indicated that the observed improvement in dysphagia is from Parts A and B is representative of a clinically meaningful within-subject improvement.

### Prurigo Nodularis

The prurigo nodularis (PN) development program included two 24-week randomized, double-blind, placebo-controlled, multicenter, parallel-group trials (PRIME (NCT04183335) and PRIME 2 (NCT04202679)) in 311 adult subjects 18 years of age and older with PN (WI-NRS ≥7 on a scale of 0 to 10) and greater than or equal to 20 nodular lesions. PRIME and PRIME 2 assessed the effect of DUXIPENT on pruritus improvement as well as its effect on PN lesions.

In these two trials, subjects received either subcutaneous DUXIPENT 600 mg (two 300 mg injections) on day 1, followed by 300 mg once every other week (Q2W) for 24 weeks, or matching placebo.

In subjects with co-morbid asthma, improvements in pre-bronchodilator FEV₁ were similar to subjects in the asthma program.

### Efficacy Results for PRIME and PRIME2 are presented in Table 23 and Figures 14, 15 and 16.
### Table 23: Efficacy Results of DUPIXENT in PRIME and PRIME2

<table>
<thead>
<tr>
<th></th>
<th>PRIME</th>
<th></th>
<th>DIFFERENCE (95% CI) for DUPIXENT vs. Placebo</th>
<th>PRIME2</th>
<th></th>
<th>DIFFERENCE (95% CI) for DUPIXENT vs. Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>9.2%</td>
<td>38.7%</td>
<td>29.6% (16.4, 42.8)</td>
<td>8.5%</td>
<td>32.1%</td>
<td>25.5% (13.1, 37.9)</td>
</tr>
<tr>
<td>DUPIXENT 300 mg Q2W</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(N=76)</td>
<td></td>
<td></td>
<td></td>
<td>(N=82)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proportion of subjects with both an improvement (reduction) in WI-NRS by ≥4 points from baseline to Week 24 a &amp; b</td>
<td>18.4%</td>
<td>60.0%</td>
<td>42.7% (27.8, 57.7)</td>
<td>19.5%</td>
<td>57.7%</td>
<td>42.6% (28.1, 56.1)</td>
</tr>
<tr>
<td>Proportion of subjects with improvement (reduction) in WI-NRS by ≥4 points from baseline at Week 24 b</td>
<td>18.4%</td>
<td>48.0%</td>
<td>28.3% (13.4, 43.2)</td>
<td>15.9%</td>
<td>44.9%</td>
<td>30.8% (16.4, 45.2)</td>
</tr>
<tr>
<td>Proportion of subjects with IGA PN-S 0 or 1 at Week 24 b</td>
<td>15.8%</td>
<td>44.0%</td>
<td>29.2% (14.5, 43.8)</td>
<td>22.0%</td>
<td>37.2%</td>
<td>16.8% (2.3, 31.2)</td>
</tr>
<tr>
<td>Proportion of subjects with improvement (reduction) in WI-NRS by ≥4 points from baseline at Week 12 a</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a Not adjusted for multiplicity in PRIME.

b Subjects who received rescue treatment earlier or had missing data were considered as non-responders.

Figure 14: Proportion of Adult Subjects with PN with Both WI-NRS ≥4-point Improvement and IGA PN-S 0 or 1 Over Time in PRIME and PRIME2

Figure 15: Proportion of Adult Subjects with WI-NRS ≥4-point Improvement Over Time in PRIME and PRIME2

Figure 16: Proportion of Adult Subjects with IGA PN-S 0 or 1 Over Time in PRIME and PRIME2

The efficacy data did not show differential treatment effect across demographic subgroups.

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### 16 HOW SUPPLIED/STORAGE AND HANDLING

**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 or pre-filled pens.

The pre-filled syringe with needle shield is designed to deliver:
- 300 mg of DUPIXENT in 2 mL solution (NDC 0024-5914-00)
- 200 mg of DUPIXENT in 1.14 mL solution (NDC 0024-5918-00)

The pre-filled pen is designed to deliver:
- 300 mg of DUPIXENT in 2 mL solution (NDC 0024-5915-00)
- 200 mg of DUPIXENT in 1.14 mL solution (NDC 0024-5919-00)

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

<table>
<thead>
<tr>
<th>Pack Size</th>
<th>300 mg/2 mL Pre-filled Syringe with Needle Shield</th>
<th>200 mg/1.14 mL Pre-filled Syringe with Needle Shield</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pack of 2 syringes</td>
<td>NDC 0024-5914-01</td>
<td>NDC 0024-5918-01</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pack Size</th>
<th>300 mg/2 mL Pre-filled Pen</th>
<th>200 mg/1.14 mL Pre-filled Pen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pack of 2 pens</td>
<td>NDC 0024-5915-02</td>
<td>NDC 0024-5919-02</td>
</tr>
</tbody>
</table>

**Storage and Handling**

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

Store refrigerated at 2°C to 8°C (36°F to 46°F) in the original carton to protect from light. If necessary, DUPIXENT may be kept at room temperature up to 25°C (77°F) for a maximum of 14 days. Do not store above 25°C (77°F). After removal from the refrigerator, DUPIXENT must be used within 14 days or discarded.

Do not expose DUPIXENT 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 and advise patients about how they may enroll 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 Dosage and Administration (2.1) and 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 healthcare provider. 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 co-morbid asthma not to adjust or stop their asthma treatment without talking to their healthcare providers [see Warnings and Precautions (5.6)].

 Arthralgia
Advise patients to report new onset or worsening joint symptoms to their healthcare provider [see Warnings and Precautions (5.7)].

 Parasitic (Helminth) Infections
Advise patients to notify their healthcare provider if they present with clinical features consistent with helminthic infection [see Warnings and Precautions (5.8)].

 Vaccinations
Advise patients that vaccination with live vaccines is not recommended immediately prior to and while they are receiving DUPIXENT. Instruct patients to inform their healthcare provider that they are taking DUPIXENT prior to a potential vaccination [see Warnings and Precautions (5.9)].

Manufactured by:
Regeneron Pharmaceuticals, Inc.
Tarrytown, NY 10591
U.S. License No. 1760
Marketed by:
sanofi-aventis U.S. LLC (Bridgewater, NJ 08807) and
Regeneron Pharmaceuticals, Inc. (Tarrytown, NY 10591)
For patent information: www.dupixent-patents.com
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REGENERON sanofi
What is DUPIXENT?

DUPIXENT is a prescription medicine used:

- to treat adults and children 6 months of age and older with moderate-to-severe eczema (atopic dermatitis or AD) that is not well controlled with prescription therapies used on the skin (topical), or who cannot use topical therapies. DUPIXENT can be used with or without topical corticosteroids.
- with other asthma medicines for the maintenance treatment of moderate-to-severe asthma in adults and children 6 years of age and older whose asthma is not controlled with their current asthma medicines. DUPIXENT helps prevent severe asthma attacks (exacerbations) and can improve your breathing. DUPIXENT may also help reduce the amount of oral corticosteroids you need while preventing severe asthma attacks and improving your breathing. DUPIXENT is not used to treat sudden breathing problems.
- with other medicines for the maintenance treatment of chronic rhinosinusitis with nasal polyposis (CRSwNP) in adults whose disease is not controlled.
- to treat adults and children 12 years of age and older, who weigh at least 88 pounds (40 kg), with eosinophilic esophagitis (EoE).
- to treat adults with prurigo nodularis (PN).

- DUPIXENT works by blocking two proteins that contribute to a type of inflammation that plays a major role in atopic dermatitis, asthma, chronic rhinosinusitis with nasal polyposis, eosinophilic esophagitis, and prurigo nodularis.
- It is not known if DUPIXENT is safe and effective in children with atopic dermatitis under 6 months of age.
- It is not known if DUPIXENT is safe and effective in children with asthma under 6 years of age.
- It is not known if DUPIXENT is safe and effective in children with chronic rhinosinusitis with nasal polyposis under 18 years of age.
- It is not known if DUPIXENT is safe and effective in children with eosinophilic esophagitis under 12 years of age and who weigh at least 88 pounds (40 kg).
- It is not known if DUPIXENT is safe and effective in children with prurigo nodularis under 18 years of age.

Do not use DUPIXENT if you are allergic to dupilumab or to any of the ingredients in DUPIXENT. See the end of this leaflet for a complete list of ingredients in DUPIXENT.

Before using DUPIXENT, tell your healthcare provider about all your medical conditions, including if you:

- have eye problems.
- have a parasitic (helminth) infection.
- are scheduled to receive any vaccinations. You should not receive a "live vaccine" right before and during treatment with DUPIXENT.
- are pregnant or plan to become pregnant. It is not known whether DUPIXENT will harm your unborn baby.

**Pregnancy Exposure Registry.** There is a pregnancy exposure registry for women who use DUPIXENT during pregnancy. The purpose of this registry is to collect information about the health of you and your baby. Your healthcare provider can enroll you in this registry. You may also enroll yourself or get more information about the registry by calling 1-877-311-8972 or going to https://mothertobaby.org/ongoing-study/dupixent/.

- are breastfeeding or plan to breastfeed. It is not known whether DUPIXENT passes into your breast milk.

Tell your healthcare provider about all of the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

**Especially tell your healthcare provider if you:**

- are taking oral, topical, or inhaled corticosteroid medicines
- have asthma and use an asthma medicine
- have atopic dermatitis, chronic rhinosinusitis with nasal polyposis, eosinophilic esophagitis, or prurigo nodularis and also have asthma

**Do not** change or stop your corticosteroid medicine or other asthma medicine without talking to your healthcare provider. This may cause other symptoms that were controlled by the corticosteroid medicine or other asthma medicine to come back.

How should I use DUPIXENT?

- See the detailed “Instructions for Use” that comes with DUPIXENT for information on how to prepare and inject DUPIXENT and how to properly store and throw away (dispose of) used DUPIXENT pre-filled syringes and pre-filled pens.
- Use DUPIXENT exactly as prescribed by your healthcare provider.
- Your healthcare provider will tell you how much DUPIXENT to inject and how often to inject it.
- DUPIXENT comes as a single-dose pre-filled syringe with needle shield or as a pre-filled pen.
  - The DUPIXENT pre-filled pen is only for use in adults and children 2 years of age and older.
  - The DUPIXENT pre-filled syringe is for use in adults and children 6 months of age and older.
- DUPIXENT is given as an injection under the skin (subcutaneous injection).
- If your healthcare provider decides that you or a caregiver can give the injections of DUPIXENT, you or your caregiver should receive training on the right way to prepare and inject DUPIXENT. Do not try to inject DUPIXENT until you have been shown the right way by your healthcare provider. In children 12 years of age and older, it is recommended that DUPIXENT be given by or under the supervision of an adult. In children 6 months to less than 12 years of age, DUPIXENT should be given by a caregiver.
- **If your dose schedule is every week and you miss a dose of DUPIXENT:** Give the DUPIXENT injection as soon as possible and start a new every week dose schedule from the time you remember to take your DUPIXENT injection.
- **If your dose schedule is every other week and you miss a dose of DUPIXENT:** Give the DUPIXENT injection within 7 days from the missed dose, then continue with your original schedule. If the missed dose is not given within 7 days, wait until the next scheduled dose to give your DUPIXENT injection.
- **If your dose schedule is every 4 weeks and you miss a dose of DUPIXENT:** Give the DUPIXENT injection within 7 days from the missed dose, then continue with your original schedule. If the missed dose is not given within 7 days, start a new every 4 week dose schedule from the time you remember to take your DUPIXENT injection.
- If you inject too much DUPIXENT (overdose), get medical help or contact a Poison Center expert right away at 1-800-222-1222.
- Your healthcare provider may prescribe other medicines to use with DUPIXENT. Use the other prescribed medicines exactly as your healthcare provider tells you to.
What are the possible side effects of DUPIXENT?
DUPIXENT can cause serious side effects, including:

- **Allergic reactions.** DUPIXENT can cause allergic reactions that can sometimes be severe. Stop using DUPIXENT and tell your healthcare provider or get emergency help right away if you get any of the following signs or symptoms:
  - breathing problems or wheezing
  - fast pulse
  - fever
  - general ill feeling
  - swollen lymph nodes
  - swelling of the face, lips, mouth, tongue, or throat
  - hives
  - itching
  - cramps in your stomach-area

- **Eye problems.** Tell your healthcare provider if you have any new or worsening eye problems, including eye pain or changes in vision, such as blurred vision. Your healthcare provider may send you to an ophthalmologist for an eye exam if needed.

- **Inflammation of your blood vessels.** Rarely, this can happen in people with asthma who receive DUPIXENT. This may happen in people who also take a steroid medicine by mouth that is being stopped or the dose is being lowered. It is not known whether this is caused by DUPIXENT. Tell your healthcare provider right away if you have:
  - rash
  - worsening shortness of breath
  - persistent fever

- **Joint aches and pain.** Joint aches and pain can happen in people who use DUPIXENT. Some people have had trouble walking or moving due to their joint symptoms, and in some cases needed to be hospitalized. Tell your healthcare provider about any new or worsening joint symptoms. Your healthcare provider may stop DUPIXENT if you develop joint symptoms.

The most common side effects of DUPIXENT include:

- injection site reactions
- upper respiratory tract infections
- eye and eyelid inflammation, including redness, swelling, and itching, sometimes with blurred vision
- herpes virus infections
- common cold symptoms (nasopharyngitis)
- cold sore in your mouth or on your lips
- high count of a certain white blood cell (eosinophilia)
- dizziness
- muscle pain
- diarrhea
- pain in the throat (oropharyngeal pain)
- gastritis
- joint pain (arthralgia)
- trouble sleeping (insomnia)
- toothache
- parasitic (helminth) infections

The following additional side effects have been reported with DUPIXENT:

- facial rash or redness

Tell your healthcare provider if you have any side effect that bothers you or that does not go away. These are not all of the possible side effects of DUPIXENT. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store DUPIXENT?
- Store DUPIXENT in the refrigerator at 36°F to 46°F (2°C to 8°C).
- Store DUPIXENT in the original carton to protect from light.
- DUPIXENT can be stored at room temperature up to 77°F (25°C) up to 14 days. Throw away (dispose of) any DUPIXENT that has been left at room temperature for longer than 14 days.
- Do not heat or put DUPIXENT into direct sunlight.
- Do not freeze. Do not shake.

Keep DUPIXENT and all medicines out of the reach of children.

General information about the safe and effective use of DUPIXENT.
Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use DUPIXENT for a condition for which it was not prescribed. Do not give DUPIXENT to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about DUPIXENT that is written for health professionals.

What are the ingredients in DUPIXENT?
Active ingredient: dupilumab
Inactive ingredients: L-arginine hydrochloride, L-histidine, polysorbate 80, sodium acetate, sucrose, and water for injection.

**REGENERON sanofi**
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For more information about DUPIXENT, go to www.DUPIXENT.com or call 1-844-DUPIXENT (1-844-387-4936).

This Patient Information has been approved by the U.S. Food and Drug Administration. Revised: October 2022