**Indications and Usage**

- **Atopic Dermatitis**
  
  DUPIXENT is an interleukin-4 receptor alpha antagonist indicated for the treatment of adult and pediatric patients aged 6 months and older with moderate-to-severe AD whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. DUPIXENT can be used with or without topical corticosteroids. (1.1)

- **Asthma**
  
  as an add-on maintenance treatment of adult and pediatric patients aged 6 years and older with moderate-to-severe asthma characterized by an eosinophilic phenotype or with oral corticosteroid dependent asthma. (1.2)

- **Chronic Rhinosinusitis with Nasal Polyposis**
  
  as an add-on maintenance treatment in adult patients with inadequately controlled chronic rhinosinusitis with nasal polyposis (CRSwNP). (1.3)

- **Eosinophilic Esophagitis**
  
  for the treatment of adult and pediatric patients aged 12 years and older, weighing at least 40 kg, with eosinophilic esophagitis (EoE). (1.4)

- **Prurigo Nodularis**
  
  for the treatment of adult patients with prurigo nodularis (PN). (1.5)

**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 given every other week (Q2W).
  
  **Dosage in Pediatric Patients 6 Months to 5 Years of Age (2.4):**
  
  Body Weight | Initial and Subsequent Dosage
  --- | ---
  5 to less than 15 kg | 200 mg (one 200 mg injection) every 4 weeks (Q4W)
  15 to less than 30 kg | 300 mg (one 300 mg injection) every 4 weeks (Q4W)

- **Dosage in Pediatric Patients 6 Years to 17 Years of Age (2.3):**
  
  Body Weight | Initial Loading Dose | Subsequent Dosage
  --- | --- | ---
  15 to less than 30 kg | 600 mg (two 300 mg injections) | 300 mg Q4W
  30 to less than 60 kg | 400 mg (two 200 mg injections) | 200 mg Q2W
  60 kg or more | 600 mg (two 300 mg injections) | 300 mg Q2W

  * Q2W – every other week; Q4W – every 4 weeks

**Recent Major Changes**

DUPIXENT is an interleukin-4 receptor alpha antagonist indicated:

**Recent Major Changes**

- **Chronic Rhinosinusitis with Nasal Polyposis (2.7):**
  
  Recommended dosage for adult patients is 600 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 given every week (QW).

- **Prurigo Nodularis (2.7):**
  
  Recommended dosage for adult patients is an initial dose of 600 mg (two 300 mg injections), followed by 300 mg given every other week (Q2W).

**Dosage Forms and Strengths**

**Single-Dose Pre-Filled Syringe with Needle Shield (3):**

- Injection: 300 mg/2 mL
- Injection: 400 mg/1.14 mL
- Injection: 100 mg/0.67 mL

**Single-Dose Pre-Filled Pen (3):**

- Injection: 300 mg/2 mL
- Injection: 200 mg/1.14 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)
- **Conjunctivitis and Keratitis:** Advise patients to report new onset or worsening eye symptoms to their healthcare provider. Consider ophthalmological examination, as appropriate. (5.2)
- **Eosinophilic Conditions:** Be alert to vasculitic rash, worsening pulmonary symptoms, and/or neuropathy, especially upon reduction of oral corticosteroids. (5.3)
- **Reduction of Corticosteroid Dosage:** Do not discontinue systemic, topical, or inhaled corticosteroids abruptly upon initiation of 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)
- **Parasitic (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)
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### Adverse Reactions

Most common adverse reactions are:

- Atopic Dermatitis (incidence ≥1%): injection site reactions, conjunctivitis, blepharitis, oral herpes, keratitis, eye pruritis, 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)

### Use of Pre-filled Pen or Pre-filled Syringe

The DUPIXENT pre-filled pen is for use in adult and pediatric patients aged 12 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 pen. In pediatric patients 12 to 17 years of age, administer DUPIXENT under the supervision of an adult. In pediatric patients 6 months to 11 years of age, administer DUPIXENT pre-filled syringe by a caregiver.

**Administration Instructions**

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

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

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

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

**2.2 Vaccination Prior to Treatment**

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

**2.3 Recommended Dosage for Atopic Dermatitis**

**Dosage in Adults**

The recommended dosage of DUPIXENT for adult patients is an initial dose of 600 mg (two 300 mg injections) followed by 300 mg given every other week (Q2W).
Dosage in Pediatric Patients 6 Months to 5 Years of Age

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

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

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>Initial* and Subsequent Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 to less than 15 kg</td>
<td>200 mg (one 200 mg injection) every 4 weeks (Q4W)</td>
</tr>
<tr>
<td>15 to less than 30 kg</td>
<td>300 mg (one 300 mg injection) every 4 weeks (Q4W)</td>
</tr>
</tbody>
</table>

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

Dosage in Pediatric Patients 6 Years to 17 Years of Age

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

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

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>Initial Loading Dose Subsequent Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>15 to less than 30 kg</td>
<td>600 mg (two 300 mg injections) every 2 weeks (Q2W)</td>
</tr>
<tr>
<td>30 to less than 60 kg</td>
<td>400 mg (two 200 mg injections) every other week (Q2W)</td>
</tr>
<tr>
<td>60 kg or more</td>
<td>600 mg (two 300 mg injections) every other week (Q2W)</td>
</tr>
</tbody>
</table>

Concomitant Topical Therapies

DUXIPENT 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 DUXIPENT for adult and pediatric patients 12 years of age and older is specified in Table 3.

Table 3: Dosage of DUXIPENT 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></td>
</tr>
<tr>
<td>600 mg (two 300 mg injections)</td>
<td>300 mg every 2 weeks (Q2W)</td>
</tr>
</tbody>
</table>

Dosage for patients with oral corticosteroid-dependent asthma or with co-morbid moderate-to-severe atopic dermatitis or adults with co-morbid chronic rhinosinusitis with nasal polyposis

600 mg (two 300 mg injections) every 2 weeks (Q2W)

Dosage in Pediatric Patients 6 to 11 Years of Age

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

Table 4: Dosage of DUXIPENT 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>100 mg every other week (Q2W)</td>
</tr>
<tr>
<td>or</td>
<td>300 mg every four 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 DUXIPENT for adult patients is 300 mg given every other week.

2.6 Recommended Dosage for Eosinophilic Esophagitis

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

2.8 Missed Doses

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

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

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

2.9 Preparation for Use

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

Inspect DUXIPENT visually for particulate matter and discoloration prior to administration. DUXIPENT 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). DUXIPENT does not contain preservatives; therefore, discard any unused product remaining in the pre-filled syringe or pre-filled pen.

3 DOSAGE FORMS AND STRENGTHS

DUXIPENT is a clear to slightly opalescent, colorless to pale yellow solution in a: Single-dose pre-filled syringe with needle shield as:

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

Single-dose pre-filled pen as:

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

4 CONTRAINDICATIONS

DUXIPENT is contraindicated in patients who have known hypersensitivity to dupilumab or any excipients of DUXIPENT [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. A clinically significant hypersensitivity reaction occurs, institute appropriate therapy and discontinue DUXIPENT [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 DUXIPENT 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 DUXIPENT 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 DUXIPENT and placebo [see Adverse Reactions (6.1)]. Among subjects with EoE, the frequency of conjunctivitis and keratitis was 0% and 0% in the DUXIPENT group and 2% and 0% in the placebo group, respectively [see Adverse Reactions (6.1)]. In subjects with PN, the frequency of conjunctivitis was 4% in the DUXIPENT group compared to 1% in the placebo group; these subjects recovered or were recovering during the treatment period. There were no cases of keratitis reported in the PN development program [see Adverse Reactions (6.1)]. Conjunctivitis and keratitis adverse events have also been reported with DUXIPENT 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 DUXIPENT 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 DUXIPENT and these conditions has not been established.
5.4 Acute Asthma Symptoms or Deteriorating Disease

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

5.5 Risk Associated with Abrupt Reduction of Corticosteroid Dosage

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

5.6 Patients with Co-morbid Asthma

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

5.7 Arthralgia

Arthralgia has been reported with the use of DUPIXENT with some patients reporting gait disturbances or decreased mobility associated with joint symptoms; some cases resulted in hospitalization. In postmarketing reports, onset of arthralgia was variable, ranging from days to months after the first dose of DUPIXENT. Some patients' symptoms resolved while continuing treatment with DUPIXENT and other patients recovered or were recovering following discontinuation of DUPIXENT.

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

5.8 Parasitic (Helminth) Infections

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

Treat patients with pre-existing helminth infections before initiating therapy with DUPIXENT. DUPIXENT with concomitant TCS infected 1/6 of subjects who received 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. Consider completing all age-appropriate vaccinations as recommended by current immunization guidelines prior to initiating treatment with DUPIXENT. Avoid use of live vaccines in patients treated with DUPIXENT. It is unknown if administration of live vaccines during DUPIXENT treatment will impact the safety or effectiveness of these vaccines. Limited data are available regarding coadministration of DUPIXENT with non-live vaccines.

6 ADVERSE REACTIONS

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

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

6.1 Clinical Trials Experience

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

Adults with Atopic Dermatitis

Three randomized, double-blind, placebo-controlled, multicenter trials (SOLO 1, SOLO 2, and CHRONOS) and one dose-ranging trial (AD-1021) evaluated the safety of DUPIXENT in subjects with moderate-to-severe AD. The safety population had a mean age of 38 years; 41% of subjects were female, 67% were White, 24% were Asian, and 6% were Black; in terms of co-morbid conditions, 48% of the subjects had asthma, 49% had allergic rhinitis, 37% had food allergy, and 27% had allergic conjunctivitis. In these 4 trials, 1472 subjects were treated with subcutaneous injections of DUPIXENT, with or without concomitant topical corticosteroids (TCS). A total of 739 subjects were treated with DUPIXENT for at least 1 year in the development program for moderate-to-severe AD.

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

AD-1225 is a multicenter, open-label extension (OLE) study which assessed the long-term safety and efficacy of DUPIXENT in 267 subjects, including 2254 exposed for at least 52 weeks, 1192 exposed for at least 100 weeks, and 357 exposed for at least 148 weeks. In AD-1225, 99.7% of subjects were exposed to DUPIXENT 300 mg weekly dosing (QW).

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

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

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

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>DUPIXENT Monotherapya</th>
<th>DUPIXENT + TCSb</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DUPIXENT 300 mg Q2W</td>
<td>Placebo</td>
</tr>
<tr>
<td>Injection site reaction</td>
<td>51 (10)</td>
<td>28 (5)</td>
</tr>
<tr>
<td>Conjunctivitisc</td>
<td>51 (10)</td>
<td>12 (2)</td>
</tr>
<tr>
<td>Blepharitisc</td>
<td>2 (&lt;1)</td>
<td>1 (&lt;1)</td>
</tr>
<tr>
<td>Oral herpesc</td>
<td>20 (4)</td>
<td>8 (2)</td>
</tr>
<tr>
<td>Keratitisc</td>
<td>1 (&lt;1)</td>
<td>0</td>
</tr>
<tr>
<td>Eye pruritusc</td>
<td>3 (1)</td>
<td>1 (&lt;1)</td>
</tr>
<tr>
<td>Other herpes simplex virus infectionc</td>
<td>10 (2)</td>
<td>6 (1)</td>
</tr>
<tr>
<td>Dry eye</td>
<td>1 (&lt;1)</td>
<td>0</td>
</tr>
</tbody>
</table>

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

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 148 Weeks (AD-1225)

The long-term safety profile observed in this trial through 148 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-1526). 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 severe AD (AD-1652). 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 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 this study, 110 (30%) had moderate 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 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 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)].
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 (DRI12544, QUEST, and VENTURE). Of these, 2678 had a history of 1 or more severe exacerbations in the year prior to enrollment despite regular use of medium to high-dose inhaled corticosteroids plus an additional controller(s) (DRI12544 and QUEST). 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>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DUPIXENT 200 mg Q2W</td>
</tr>
<tr>
<td></td>
<td>N=779 n (%)</td>
</tr>
<tr>
<td>Injection site reactions</td>
<td>111 (14%)</td>
</tr>
<tr>
<td>Ororhyngeal pain</td>
<td>13 (2%)</td>
</tr>
<tr>
<td>Eosinophilia</td>
<td>17 (2%)</td>
</tr>
</tbody>
</table>

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>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DUPIXENT 300 mg Q2W</td>
</tr>
<tr>
<td></td>
<td>N=440 n (%)</td>
</tr>
<tr>
<td>Injection site reactions</td>
<td>28 (6%)</td>
</tr>
<tr>
<td>Conjonctivitis</td>
<td>7 (2%)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>14 (3%)</td>
</tr>
</tbody>
</table>

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, with EsoE were evaluated in a randomized, double-blind, parallel-group, multicenter, placebo-controlled trial, including 24-week treatment periods (Parts A and B) and received either DUPIXENT 300 mg QW or placebo (see Clinical Studies (14.4)).

The proportion of subjects who discontinued treatment due to adverse events was 2% of the placebo group and 2% of the DUPIXENT 300 mg QW group.

Table 8 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 Parts A and B.

### 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></td>
<td>N=122 n (%)</td>
<td>N=117 n (%)</td>
</tr>
<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>3 (2%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Herpes viral infections</td>
<td>3 (2%)</td>
<td>1 (1%)</td>
</tr>
</tbody>
</table>

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 2 randomized, double-blind, placebo-controlled, multicenter trials (PRIME and PRIME2). The safety profile 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.

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 ≥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>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DUPIXENT 300 mg Q2W</td>
</tr>
<tr>
<td></td>
<td>N=440 n (%)</td>
</tr>
<tr>
<td>Gastritis</td>
<td>7 (2%)</td>
</tr>
<tr>
<td>Insomnia</td>
<td>6 (1%)</td>
</tr>
<tr>
<td>Eosinophilia</td>
<td>5 (1%)</td>
</tr>
<tr>
<td>Toothache</td>
<td>5 (1%)</td>
</tr>
</tbody>
</table>

* Injection site reactions cluster includes injection site reaction, pain, bruising and swelling.
* 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.
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></td>
<td>DUPIXENT 300 mg Q2W</td>
<td>N=152 n (%)</td>
</tr>
<tr>
<td>Nasopharyngitisa</td>
<td>8 (5%)</td>
<td>3 (2%)</td>
</tr>
<tr>
<td>Conjunctivitisb</td>
<td>6 (4%)</td>
<td>2 (1%)</td>
</tr>
<tr>
<td>Herpes Infectionc</td>
<td>5 (3%)</td>
<td>0%</td>
</tr>
<tr>
<td>Dizzinessd</td>
<td>5 (3%)</td>
<td>2 (1%)</td>
</tr>
<tr>
<td>Myalgiaa</td>
<td>5 (3%)</td>
<td>2 (1%)</td>
</tr>
<tr>
<td>Diarrheaa</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 group (29 per 100 subject-years) and in 9% of the placebo + TCS group (10 per 100 subject-years). During the long-term OLE trial with data through 148 weeks (AD-1225), conjunctivitis was reported in 20% of the DUPIXENT group (12 per 100 subject-years).

In DUPIXENT AD monotherapy trials (SOLO 1, SOLO 2, and AD-1021) through Week 16, keratitis was reported in <1% of the DUPIXENT group (1 per 100 subject-years) and in 0% of the placebo group (0 per 100 subject-years). In the 52-week DUPIXENT + topical corticosteroids (TCS) AD trial (CHRONOS), keratitis was reported in 4% of the DUPIXENT + TCS group (4 per 100 subject-years) and in 2% of the placebo + TCS group (2 per 100 subject-years). Conjunctivitis and keratitis occurred more frequently in AD subjects who received DUPIXENT. Conjunctivitis was the most frequently reported eye disorder. During the long-term OLE trial with data through 148 weeks (AD-1225), keratitis was reported in 3% of the DUPIXENT group (2 per 100 subject-years). Most subjects with conjunctivitis or keratitis recovered or were recovering during the treatment period.

Among subjects with asthma, the frequency of conjunctivitis and keratitis was similar between DUPIXENT and placebo.

In subjects with CRSwNP, the frequency of conjunctivitis was 2% in the DUPIXENT group compared to 1% in the placebo group in the 24-week safety pool; these subjects recovered.

In the 52-week CRSwNP study (SINUS-52), the frequency of conjunctivitis was 3% in the DUPIXENT subjects and 1% in the placebo subjects; all of these subjects recovered. There were no cases of keratitis reported in the CRSwNP development program [see Warnings and Precautions (5.2)].

Among subjects with EoE, the frequency of conjunctivitis and keratitis was 0% and 0% in the DUPIXENT group and 2% and 0% in the placebo group, respectively.

Among subjects with PN, the frequency of conjunctivitis was 4% in the DUPIXENT group compared to 1% in the placebo group; all of these subjects recovered or were recovering during the treatment period. There were no cases of keratitis reported in the PN development program [see Warnings and Precautions (5.2)].

Eczema Herpeticum and Herpes Zoster

The rate of eczema herpeticum was similar in the placebo and DUPIXENT groups in the AD trials. The rates remained stable through 148 weeks in the long-term OLE trial (AD-1225).

Herpes zoster was reported in <1% of the DUPIXENT groups (1 per 100 subject-years) and in <1% of the placebo group (1 per 100 subject-years) in the 16-week AD monotherapy trials. In the 52-week DUPIXENT + TCS AD trial, herpes zoster was reported in 1% of the DUPIXENT + TCS group (1 per 100 subject-years) and 2% of the placebo + TCS group (2 per 100 subject-years). During the long-term OLE trial with data through 148 weeks (AD-1225), 1.9% of DUPIXENT-treated subjects reported herpes zoster (0.99 per 100 subject-years). Most subjects with herpes zoster or ophthalmic herpes zoster were reported in <1% of the DUPIXENT group (1 per 100 subject-years) and 0% of the placebo group.

Hypersensitivity Reactions

Hypersensitivity reactions were reported in <1% of DUPIXENT-treated subjects. These included anaphylaxis, serum sickness or serum sickness-like reactions, generalized urticaria, rash, erythema nodosum, and erythema multiforme [see Contraindications (4), Warnings and Precautions (5.1), and Adverse Reactions (6.2)].
Skin and subcutaneous tissue disorders:

Two adult subjects with AD who experienced high titer antibody responses developed

The antibody titers detected in subjects who received DUPIXENT were mostly low. In subjects who received DUPIXENT, development of high titer antibodies to DUPIXENT was associated with lower serum dupilumab concentrations [see Clinical Pharmacology (12.3)].

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

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to DUPIXENT during pregnancy. Healthcare providers and patients may call 1-877-311-8972 or go to https://mothertotbaby.org/ongoing-study/dupixent/ to enroll in or to obtain information about the registry.

Risk Summary

Available data from case reports and case series with DUPIXENT use in pregnant women have not identified a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Human IgG antibodies are known to cross the placental barrier; therefore, DUPIXENT may be transmitted from the mother to the developing fetus. In women with poorly or moderately controlled asthma, evidence demonstrates that there is an increased risk of preeclampsia in the mother and premature, low birth weight, and small for gestational age in the neonate. The level of asthma control should be closely monitored in pregnant women and treatment adjusted as necessary to maintain optimal control.

Clinical Considerations

Disease-Associated Maternal and/or Embryo-fetal Risk

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

Data

Animal Data

In an enhanced pre- and post-natal development toxicity study, pregnant cynomolgus monkeys were administered weekly subcutaneous doses of homologous antibody against IL-4Rα during organogenesis through parturition at doses up to 10-times the maximum recommended human dose (MRHD) [see Data].

The background risk of major birth defects and miscarriage for the indicated populations are unknown. All pregnancies have a background risk of birth defect, loss or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations

Disease-Associated Maternal and/or Embryo-fetal Risk

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

Data

Animal Data

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

8.2 Lactation

Risk Summary

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

8.4 Pediatric Use

Atopic Dermatitis

The safety and effectiveness of DUPIXENT have been established in pediatric patients 6 months of age and older with moderate-to-severe AD [see Clinical Studies (14.1)].

Use of DUPIXENT in this age group is supported by data from the following clinical trials:

• AD-1526 which included 251 pediatric subjects 12 to 17 years of age with moderate-to-severe AD treated with DUPIXENT + TCS
• AD-1539 which included 161 pediatric subjects 6 months to 5 years of age with moderate-to-severe AD treated with DUPIXENT + TCS
• AD-1434, an open-label extension study that enrolled 275 pediatric subjects 12 to 17 years of age treated with DUPIXENT, 366 pediatric subjects 6 to 11 years of age treated with DUPIXENT + TCS, and 180 pediatric subjects 6 months to 5 years of age treated with DUPIXENT + TCS

The safety and effectiveness were generally consistent between pediatric and adult patients [see Adverse Reactions (6.1) and Clinical Studies (14.1)]. In addition, hand-foot-mouth disease was reported in 9 (5%) pediatric subjects and skin papilloma was reported in 5 (3%) pediatric subjects 6 months to 5 years of age treated with DUPIXENT + TCS in AD-1434. These cases did not lead to study drug discontinuation. [see Adverse Reactions (6.1)].

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

Asthma

The safety and effectiveness of DUPIXENT for an add-on maintenance treatment in patients with moderate-to-severe asthma characterized by an eosinophilic phenotype or with oral corticosteroid dependent asthma have been established in pediatric patients 6 years of age and older. Use of DUPIXENT for this indication is supported by evidence from adequate and well-controlled studies in adult and pediatric patients 6 years and older [see Clinical Studies (14.2)].

Pediatric Subjects 12 to 17 Years of Age:

A total of 107 pediatric subjects 12 to 17 years of age with moderate-to-severe asthma were enrolled in QUEST and received either 200 mg (N=21) or 300 mg (N=18) DUPIXENT (or matching placebo either 200 mg [N=34] or 300 mg [N=34]) Q2W. Asthma exacerbations and lung function were assessed in both pediatric subjects 12 to 17 years of age and adults. For both the 200 mg and 300 mg Q2W doses, improvements in FEV1 (LS mean change from baseline at Week 12) were observed (0.36 L and 0.27 L, respectively). For the 200 mg Q2W dose, subjects had a reduction in the rate of severe exacerbations that was consistent with adults. Dupilumab exposure was higher in pediatric subjects 12 to 17 years of age than that in adults at the respective dose level which was mainly accounted for by difference in body weight [see Clinical Pharmacology (12.3)].

The adverse event profile in 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. Improvement in asthma exacerbations and lung function were demonstrated [see Clinical Studies (14.2)]. The effectiveness of DUPIXENT 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 LTI1434 (Evaluating the safety and efficacy of DUPIXENT 300 mg Q4W in subjects 6 to 11 years of age with moderate-to-severe asthma). It is not possible to reliably estimate their frequency or establish a cause-and-effect relationship to drug exposure.

In addition, hand-foot-mouth disease was reported in 5 (3%) pediatric subjects 6 months to 5 years of age treated with DUPIXENT + TCS in AD-1434. These cases did not lead to study drug discontinuation. [see Adverse Reactions (6.1)].

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 DUPIXENT for the treatment of EoE have been established in pediatric patients 12 years of age and older, weighing at least 40 kg. Use of DUPIXENT in this population is supported by an adequate and well-controlled study in adults (Parts A and B) which 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 (14.4)].

The safety and effectiveness of DUPIXENT 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 Prurigo Nodularis have not been established.

8.5 Geriatric Use

Of the 1472 subjects with AD exposed to DUPIXENT in a dose-ranging study and placebo-controlled trials, 67 subjects were 65 years or older. Clinical trials of DUPIXENT 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 DUPIXENT, a total of 240 subjects were 65 years or older. Use of DUPIXENT for this indication is supported by evidence from adequate and well-controlled studies in adults and pediatric patients 6 years and older [see Clinical Studies (14.2)].

Of the 440 subjects with CRSwNP exposed to DUPIXENT, a total of 79 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 DUPIXENT, 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 DUPIXENT in EoE did not include sufficient numbers of subjects aged 65 years and over to determine whether they respond differently from younger adult subjects.
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 2-times the recommended dose).

**Weight**

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

**Immunogenicity**

Development of antibodies to dupilumab was associated with lower serum dupilumab concentrations. A few subjects who had high antibody titers also had no detectable serum dupilumab concentrations.

**Specific Populations**

**Geriatric Patients**

In subjects who are 65 years and older, the mean ± SD steady-state trough concentrations of dupilumab were 69.4±31.4 mcg/mL and 166±62.3 mcg/mL, respectively, for 300 mg administered Q2W and weekly, and 39.7±21.7 mcg/mL for 200 mg administered Q2W.

**Pediatric Patients**

**Atopic Dermatitis**

For pediatric subjects 12 to 17 years of age with AD receiving every other week dosing (Q2W) with either 200 mg (<60 kg) or 300 mg (≥60 kg), the mean ± SD steady-state trough concentration of dupilumab was 54.5±27.0 mcg/mL.

**Asthma**

A total of 107 pediatric subjects 12 to 17 years of age with asthma were enrolled in QUEST. The mean ± SD steady-state trough concentrations of dupilumab were 107±51.6 mcg/mL and 46.7±26.9 mcg/mL, respectively, for 300 mg or 200 mg administered Q2W.

In VOYAGE, dupilumab pharmacokinetics was investigated in 270 subjects with moderate-to-severe asthma following subcutaneous administration of either 100 mg Q2W (for 91 pediatric subjects weighing <30 kg) or 200 mg Q2W (for 179 pediatric subjects weighing ≥30 kg). The mean ± SD steady-state trough concentration was 58.4±28.0 mcg/mL and 85.1±44.9 mcg/mL, respectively. Simulation of a 300 mg Q4W subcutaneous dose in pediatric subjects 6 to 11 years of age with body weight of ≥15 to <30 kg resulted in predicted steady-state trough concentrations (98.7±41.0 mcg/L) and average concentrations higher than the observed trough concentrations and average concentrations of 100 mg Q2W (<30 kg).

**Eosinophilic Esophagitis**

In a clinical study (Parts A and B), dupilumab pharmacokinetics were investigated in 35 pediatric subjects 12 to 17 years of age, weighing at least 40 kg, with EoE, receiving 300 mg QW. The mean ± SD steady-state trough concentration of dupilumab was 227 ± 95.3 mcg/mL.

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

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

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

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

14 CLINICAL STUDIES

14.1 Atopic Dermatitis

Adults with Atopic Dermatitis

Three randomized, double-blind, placebo-controlled trials (SOLO 1 (NCT02277743), SOLO 2 (NCT02277769), and CHRONOS (NCT02260886)) 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 DUPIXENT group received subcutaneous injections of DUPIXENT 600 mg at Week 0, followed by 300 mg every other week (Q2W). In the monotherapy trials (SOLO 1 and SOLO 2), subjects received DUPIXENT or placebo for 16 weeks.

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

All three trials assessed the primary endpoint, the change from baseline to Week 16 in 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 (improvement of at least 75% in EASI score from baseline), and reduction in itch as defined by a reduction of ≥2 points on a 0-72 Pruritus NRS from baseline to Week 16.

Clinical Response at Week 16 (FAS)

At baseline, 46% of subjects had an IGA score of 3 (moderate AD), 54% had an IGA score of 4 (severe AD), the mean BSA involvement was 57%, and 42% had received prior immunosuppressants (e.g., 52% of DUPIXENT IGA 0 or 1 non-responders at Week 16 became responders at Week 52). Results of positive 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></th>
<th>DUPIXENT 300 mg Q2W + TCS</th>
<th>Placebo + TCS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Subjects ≥68</td>
<td>89</td>
<td>264</td>
</tr>
<tr>
<td>Responders at Week 16</td>
<td>22%</td>
<td>7%</td>
</tr>
<tr>
<td>Responders at Week 52</td>
<td>20%</td>
<td>6%</td>
</tr>
<tr>
<td>Non-responders at Week 16</td>
<td>44%</td>
<td>80%</td>
</tr>
<tr>
<td>Overall Responders at Week 52</td>
<td>36%</td>
<td>13%</td>
</tr>
</tbody>
</table>

* 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.
* 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.
* Full Analysis Set (FAS) includes all subjects randomized.
* 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.
* Responders at Week 16 were considered responders at Week 52.
* Non-responders at Week 16 were considered non-responders at Week 52.
* Overall Responder at Week 52 was considered a responder at Week 16.

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

In SOLO 1, SOLO 2, and CHRONOS, a third randomized treatment arm of DUPIXENT 300 mg Q2W did not demonstrate additional treatment benefit over DUPIXENT 300 mg Q2W.

Subjects in SOLO 1 and SOLO 2 who had an IGA 0 or 1 with a reduction of ≥2 points were re-randomized into SOLO CONTINUE (NCT02395133). SOLO CONTINUE evaluated multiple DUPIXENT monotherapy dose regimens for maintaining treatment response. The study included subjects randomized to continue with DUPIXENT 300 mg Q2W (62 subjects) or switch to placebo (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 <60 kg received an initial dose of 300 mg at Week 0, followed by 200 mg Q2W for 16 weeks. Subjects with baseline weight of ≥60 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, 46% of subjects had an IGA score of 3 (moderate AD), 54% had an IGA score of 4 (severe AD), the mean BSA involvement was 57%, and 42% had received prior immunosuppressants (e.g., 53% of DUPIXENT IGA 0 or 1 non-responders at Week 16 remained responders at Week 52) and subjects who were non-responders at Week 16 who later responded to treatment (e.g., 24% of DUPIXENT IGA 0 or 1 non-responders at Week 16 became responders at Week 52).

Results of positive analyses of the 353 subjects in the DUPIXENT with concomitant TCS trial (CHRONOS) are presented in Table 11.
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></th>
<th>DUPIXENT* 200 mg (&lt;60 kg) or 300 mg (≥60 kg) Q4W (N=85)</th>
<th>Placebo N=85*</th>
</tr>
</thead>
<tbody>
<tr>
<td>IGA 0 or 1 (clear)</td>
<td>24%</td>
<td>2%</td>
</tr>
<tr>
<td>EASI-75c</td>
<td>42%</td>
<td>8%</td>
</tr>
<tr>
<td>EASI-90c</td>
<td>23%</td>
<td>2%</td>
</tr>
<tr>
<td>Peak Pruritus NRS (≥4-point improvement)c</td>
<td>37%</td>
<td>5%</td>
</tr>
</tbody>
</table>

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

c Responder was defined as a subject with an IGA 0 or 1 ("clear" or "almost clear") and a reduction of ≥2 points on a 0-4 IGA scale.

c Subjects who received rescue treatment or with missing data were considered non-responders (59% and 21% in the placebo and DUPIXENT arms, respectively).

c At Week 0, subjects received 400 mg (baseline weight <60 kg) or 600 mg (baseline weight ≥60 kg) of DUPIXENT.

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

Figure 2: Proportion of Pediatric Subjects 12 to 17 Years of Age with Moderate-to-Severe AD with ≥4-point Improvement on the Peak Pruritus NRS in AD-1526* (FAS)b

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.

Pediatric Subjects 6 to 11 Years of Age with Atopic Dermatitis

The efficacy and safety of DUPIXENT use concomitantly with TCS in pediatric subjects was evaluated in a multicenter, randomized, double-blind, placebo-controlled trial (AD-1652; NCT03349914) 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 ≥25%. 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 DUPIXENT 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 DUPIXENT Q4W + 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%, respectively), and reduction in itch as measured by the Peak Pruritus NRS (≥4-point improvement).

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

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

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.

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

The efficacy and safety of DUPIXENT use concomitantly with TCS in pediatric subjects was evaluated in a multicenter, randomized, double-blind, placebo-controlled trial (AD-1539; NCT03346434) in 162 subjects 6 months to 5 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. Enrollment was stratified by baseline weight (≥25 to <15 kg and ≥15 to <30 kg).

Subjects in the DUPIXENT Q4W + TCS group with baseline weight of ≥25 to <15 kg received an initial dose of 200 mg on Day 1, followed by 100 mg Q2W from Week 4 to Week 12, and subjects with baseline weight of ≥15 to <30 kg received an initial dose of 300 mg on Day 1, followed by 300 mg Q4W from Week 4 to Week 12. Subjects were permitted to receive rescue treatment at the discretion of the investigator. Subjects who received rescue treatment were considered non-responders.

In AD-1539, the mean age was 3.8 years, the median weight was 16.5 kg, 39% of subjects were female, 69% were White, 19% were Black, and 6% were Asian. At baseline, the mean BSA involvement was 58%, and 29% of subjects had received prior systemic immunosuppressants. Also, at baseline the mean EASI score was 34.1, and the weekly average
of daily worst scratch/itch score was 7.6 on a scale of 0-10. Overall, 81.4% of subjects had at least one co-morbid allergic condition; 68.3% had food allergies, 52.8% had other allergies, 44.1% had allergic rhinitis, and 25.5% 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 Worst Scratch/Itch NRS (≥4-point improvement).

The efficacy results at Week 16 for AD-1539 are presented in Table 14.

Table 14: Efficacy Results of DUPIXENT with Concomitant TCS in AD-1539 at Week 16 (FAS) in Pediatric Subjects 6 Months to 5 Years of Age with Moderate-to-Severe AD

<table>
<thead>
<tr>
<th>Parameter</th>
<th>DUPIXENT + TCS</th>
<th>Placebo + TCS</th>
<th>Difference vs. Placebo (95 % CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IGA 0 or 1</td>
<td>28% (N=83)*</td>
<td>4% (N=79)*</td>
<td>24% (13%, 34%)</td>
</tr>
<tr>
<td>EASI-75</td>
<td>53%</td>
<td>11%</td>
<td>42% (29%, 55%)</td>
</tr>
<tr>
<td>EASI-90</td>
<td>25%</td>
<td>3%</td>
<td>23% (12%, 33%)</td>
</tr>
<tr>
<td>Worst Scratch/Itch NRS (≥4-point improvement)*</td>
<td>48%</td>
<td>9%</td>
<td>39% (26%, 52%)</td>
</tr>
</tbody>
</table>

CI = confidence interval

- * Full Analysis Set (FAS) includes all subjects randomized.
- # Responder was defined as a subject with an IGA 0 or 1 ("clear" or "almost clear").
- & Subjects who received rescue treatment (63% and 19% in the placebo and DUXIPENT arms, respectively) or with missing data were considered as non-responders.
- / At Day 1, subjects received 200 mg (5 to <15kg) or 300 mg (15 to <30 kg) of DUXIPENT.

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 (DRI12544 (NCT01854047), QUEST (NCT02148584), and VENTURE (NCT02528214)) of 24 to 52 weeks duration which enrolled a total of 2888 subjects. Subjects enrolled in DRI12544 and QUEST were required to have a history of 1 or more asthma exacerbations that required treatment with systemic corticosteroids or emergency department visit or hospitalization for the treatment of asthma in the year prior to trial entry. Subjects enrolled in VENTURE required dependence on daily oral corticosteroids in addition to regular use of high-dose inhaled corticosteroids plus an additional controller(s). Subjects continued background asthma control throughout the duration of the studies, except in VENTURE in which OCS dose was tapered as described below.

DRI12544

DRI12544 was a 24-week dose-ranging study which included 776 adult subjects (18 years of age and older). DUXIPENT compared with placebo was evaluated in adult subjects with moderate-to-severe asthma on a medium or high-dose inhaled corticosteroid and a longacting beta agonist. Subjects were randomized to receive either 200 mg (N=150) or 300 mg (N=157) DUXIPENT every other week (Q2W) or 200 mg (N=154) or 300 mg (N=157) DUXIPENT every 4 weeks following an initial dose of 400 mg, 600 mg or placebo (N=158), respectively. The primary endpoint was mean change from baseline to Week 12 in ACQ-5 and AQLQ(S) scores. Other endpoints included percent reduction of oral corticosteroid dose at Weeks 20 to 24 compared with baseline, weight gain, and adverse events. Subjects continued background asthma control throughout the duration of the study. In VENTURE, the overall population in QUEST, the rate of severe 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 0.87 and 0.97. The rate ratio of severe exacerbations compared to placebo was 0.52 (95% CI: 0.41, 0.66) and 0.54 (95% CI: 0.43, 0.68) for 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 eosinophil counts and baseline FeNO for QUEST are shown in 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 eosinophil counts ≥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.

The demographics and baseline characteristics of these 3 trials are provided in Table 15 below.
Table 16: Rate of Severe Exacerbations in DRI12544 and QUEST

<table>
<thead>
<tr>
<th>Trial</th>
<th>Treatment</th>
<th>Baseline Blood EOS ≥300 cells/mcL (primary analysis population, DRI12544)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Rate (95% CI)</td>
</tr>
<tr>
<td>DRI12544</td>
<td>DUPIXENT 200 mg Q2W</td>
<td>65</td>
</tr>
<tr>
<td></td>
<td>DUPIXENT 300 mg Q2W</td>
<td>64</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>68</td>
</tr>
<tr>
<td>QUEST</td>
<td>DUPIXENT 200 mg Q2W</td>
<td>264</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>148</td>
</tr>
<tr>
<td></td>
<td>DUPIXENT 300 mg Q2W</td>
<td>277</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>142</td>
</tr>
</tbody>
</table>

Significant increases in pre-bronchodilator FEV₁ were observed at Week 12 for DRI12544 and QUEST in the primary analysis populations (subjects with baseline eosinophil count of ≥300 cells/mcL in DRI12544 and the overall population in QUEST). In the overall population in QUEST, the FEV₁ LS mean change from baseline was 0.32 L (21%) and 0.34 L (23%) for DUPIXENT 200 mg Q2W and 300 mg Q2W, respectively, compared to matched placebo means of 0.18 L (12%) and 0.21 L (14%). The mean treatment difference versus placebo was 0.14 L (95% CI: 0.08, 0.19) and 0.13 L (95% CI: 0.08, 0.18) for DUPIXENT 200 mg Q2W and 300 mg Q2W, respectively. Results in subjects with baseline eosinophil counts ≥300 cells/mcL in DRI12544 and QUEST are shown in Table 17.

Improvements in FEV₁, by baseline eosinophil counts and baseline FeNO for QUEST are shown in Figure 7 and 8, respectively. Subgroup analysis of DRI12544 and QUEST demonstrated greater improvement in subjects with higher baseline eosinophil counts (≥150 cells/mcL) or FeNO (≥25 ppb). In subjects with baseline eosinophil count <150 cells/mcL and FeNO <25 ppb, similar differences in FEV₁ were observed between DUPIXENT and placebo.

Mean changes in FEV₁, over time in QUEST are shown in Figure 9.

Table 17: Mean Change from Baseline and Difference vs Placebo in Pre-Bronchodilator FEV₁ at Week 12 in Subjects with Moderate-to-Severe Asthma (DRI12544 and QUEST)

<table>
<thead>
<tr>
<th>Trial</th>
<th>Treatment</th>
<th>Baseline Blood EOS ≥300 cells/mcL (primary analysis population, DRI12544)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>LS Mean Change from baseline (95% CI)</td>
</tr>
<tr>
<td>DRI12544</td>
<td>DUPIXENT 200 mg Q2W</td>
<td>65</td>
</tr>
<tr>
<td></td>
<td>DUPIXENT 300 mg Q2W</td>
<td>64</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>68</td>
</tr>
<tr>
<td>QUEST</td>
<td>DUPIXENT 200 mg Q2W</td>
<td>264</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>148</td>
</tr>
<tr>
<td></td>
<td>DUPIXENT 300 mg Q2W</td>
<td>277</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>142</td>
</tr>
</tbody>
</table>

Lung Function

The time to first exacerbation was longer for the subjects receiving DUPIXENT compared to placebo in QUEST (Figure 6).
The key secondary endpoint was the change from baseline in pre-bronchodilator FEV₁ (L) over time in subjects with moderate-to-severe asthma with baseline blood eosinophil count ≥300 cells/mcL (QUEST).

### 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 DUXPENT 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 1.29; 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.

- The ACQ-5 responder rate for DUXPENT 200 mg and 300 mg Q2W in subjects with baseline blood eosinophils ≥300 cells/mcL was 75% vs 67% placebo (odds ratio: 1.46; 95% CI: 0.90; 2.35) and 71% vs 64% placebo (odds ratio: 1.39; 95% CI: 0.88; 2.19), respectively; and the AQLQ(S) responder rates were 71% vs 55% placebo (odds ratio: 2.02; 95% CI: 1.24; 3.26) and 65% vs 56% placebo (odds ratio: 1.79; 95% CI: 1.13; 2.65), respectively.

### Oral Corticosteroid Reduction (VENTURE)

VENTURE evaluated the effect of DUXPENT 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 DUXPENT. 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 DUXPENT 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 DUXPENT (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 82% (95% subjects receiving DUXPENT compared to 57% (53%) in those receiving placebo. The proportion of subjects with a mean final dose less than 5 mg at Week 24 was 72% for DUXPENT and 37% for placebo (odds ratio 4.48 95% CI: 2.3, 8.39). A total of 54 (52%) subjects receiving DUXPENT 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 DUXPENT compared with those receiving placebo (annualized rate 0.65 and 1.60 for the DUXPENT and placebo group, respectively; rate ratio 0.41 [95% CI 0.26, 0.63]) and improvement in pre-bronchodilator FEV₁, from baseline to Week 24 was greater in subjects receiving DUXPENT compared with those receiving placebo (LS mean difference for DUXPENT 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 ACQ-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 DUXPENT in pediatric subjects was evaluated in a 52-week multicenter, randomized, double-blind, placebo-controlled study (VOYAGE; NCT02948959) in 408 subjects 6 to 11 years of age, with moderate-to-severe asthma on ICS. A subset of these subjects had an eosinophilic phenotype as indicated by elevated blood eosinophils and/or the population was 69% vs 63% placebo (odds ratio 1.29; 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.

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

DUXPENT 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 as indicated by elevated blood eosinophils and/or the population subset with elevated FeNO. Subgroup analyses for results of DUXPENT treatment based upon either baseline eosinophil level or baseline FeNO level were similar to the pediatric (12 to 17 years of age) and adult trials and are described for the adult and pediatric (12 to 17 years of age) asthma population above. In subjects with baseline blood eosinophil count <150 cells/mL and FeNO <20 ppb, similar severe asthma exacerbation rates were observed between DUXPENT 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 DUXPENT in VOYAGE

<table>
<thead>
<tr>
<th>Treatment</th>
<th>EOS ≥300 cells/mL a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annualized Severe Exacerbations Rate over 52 Weeks</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>Rate (95% CI)</td>
</tr>
<tr>
<td>100 mg Q2W (≤30 kg)</td>
<td>175</td>
</tr>
<tr>
<td>Placebo</td>
<td>84</td>
</tr>
</tbody>
</table>

Mean Change from Baseline in Percent Predicted FEV₁, at Week 12

<table>
<thead>
<tr>
<th>N</th>
<th>LS mean from Baseline</th>
<th>LS mean difference vs. Placebo (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DUXPENT 100 mg Q2W (≤30 kg)</td>
<td>168</td>
<td>10.15</td>
</tr>
<tr>
<td>Placebo</td>
<td>80</td>
<td>4.83</td>
</tr>
</tbody>
</table>

*This reflects the prespecified primary analysis population for VOYAGE in the United States.*
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 (8)</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>
<tr>
<td>Mean LMK sinus CT total score* (SD), range 0-24</td>
<td>19 (4.4)</td>
<td>18 (3.8)</td>
</tr>
<tr>
<td>Mean loss of smell score* (AM), (SD) range 0-3</td>
<td>2.7 (0.5)</td>
<td>2.8 (0.5)</td>
</tr>
<tr>
<td>Mean SNOT-22 total score*(SD), range 0-110</td>
<td>49.4 (20.2)</td>
<td>51.9 (20.9)</td>
</tr>
<tr>
<td>Mean blood eosinophils (cells/mcL) (SD)</td>
<td>440 (330)</td>
<td>430 (350)</td>
</tr>
<tr>
<td>Mean total IgE IU/mL (SD)</td>
<td>212 (276)</td>
<td>240 (342)</td>
</tr>
<tr>
<td>Atopic Medical History % Overall</td>
<td>75</td>
<td>82</td>
</tr>
<tr>
<td>Asthma (%)</td>
<td>58</td>
<td>60</td>
</tr>
<tr>
<td>NSAID-ERD (%)</td>
<td>30</td>
<td>27</td>
</tr>
</tbody>
</table>

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

Clinical Response (SINUS-24 and SINUS-52)
The results for primary endpoints in CRSwNP studies are presented in Table 21.

TABLE 21: Results of the Primary Endpoints in CRSwNP Trials

<table>
<thead>
<tr>
<th>Primary Endpoints at Week 24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo (n=133)</td>
</tr>
<tr>
<td>LS mean difference vs. Placebo (95% CI)</td>
</tr>
<tr>
<td>LS mean change</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>NPS</th>
<th>Baseline mean</th>
<th>LS mean change</th>
<th>Baseline mean</th>
<th>LS mean change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5.86</td>
<td>0.17</td>
<td>5.64</td>
<td>-1.89</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>NC</th>
<th>Baseline mean</th>
<th>LS mean change</th>
<th>Baseline mean</th>
<th>LS mean change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2.45</td>
<td>-0.45</td>
<td>2.26</td>
<td>-1.34</td>
</tr>
</tbody>
</table>

A reduction in score indicates improvement.
NPS = nasal polyps score; NC = nasal congestion obstruction

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=partial opacification; 2=total opacification) deriving a maximum score of 12 per side and a total maximum score of 24 (higher scores indicate more opacification). Loss of smell was scored reflectively by the subject every morning on a 0-3 scale (0=no symptoms; 1=mild symptoms; 2=moderate symptoms; 3=severe symptoms). 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 had a 2 week recall period. In the pooled efficacy results, the reduction in the proportion of subjects rescued with systemic corticosteroids and/or sino-nasal surgery (up to Week 52) were evaluated.

The demographics and baseline characteristics of these 2 trials are provided in Table 20 below.
Duluxinab significantly decreased sino-nasal symptoms as measured by SNOT-22 compared to placebo. The LS mean difference for SNOT-22 at Week 24 in the DUPIXENT group versus placebo was -21.12 (95% CI: -25.17, -17.06) in SINUS-24 and -17.36 (95% CI: -20.87, -13.85) in SINUS-52. At Week 52, the LS mean difference in the DUPIXENT group versus placebo was -20.96 (95% CI: -25.03, -16.89).

In the pre-specified multiplicity-adjusted pooled analysis of two studies, treatment with DUPIXENT 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).

The effects of DUPIXENT on the primary endpoints of SNOT-22 and nasal congestion and the key secondary endpoint of LMK sinus CT scan score were consistent in subjects with prior surgery and without prior surgery.

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

### 14.4 Eosinophilic Esophagitis

A single randomized, double-blind, parallel-group, multicenter, placebo-controlled trial, including two 24-week treatment periods (Parts A and B), was conducted in adult and pediatric subjects 12 to 17 years of age, weighing at least 40 kg, with EoE (NCT03633617). In both parts, subjects were randomized to receive 300 mg DUPIXENT every week or placebo. Eligible subjects had >15 intraepithelial eosinophils per high-power field (eos/hpf) following a treatment course of a proton pump inhibitor (PPI) either prior to or during the screening period and symptoms of dysphagia as measured by the Dysphagia Symptom Questionnaire (DSQ). At baseline, 43% of subjects in Part A and 37% of subjects in Part B had a history of prior esophageal dilations.

Demographics and baseline characteristics were similar in Parts A and B. A total of 81 subjects (61 adults and 20 pediatric subjects) were enrolled in Part A and 159 subjects (107 adults and 52 pediatric subjects) were enrolled in Part B. The mean age in years was 32 years (range 13 to 62 years) in Part A and 28 years (range 12 to 66 years) in Part B. The majority of subjects were male (60% in Part A and 68% in Part B) and White (96% in Part A and 90% in Part B). The mean baseline DSQ score (SD) was 53.6 (12.4) in Part A and 37.2 (10.7) in Part B.

The majority of subjects were male (60% in Part A and 68% in Part B) and White (96% in Part A and 90% in Part B). The mean baseline DSQ score (SD) was 53.6 (12.4) in Part A and 37.2 (10.7) in Part B.

The COP primary efficacy endpoints in Parts A and B were the (1) proportion of subjects achieving histological remission defined as peak esophageal intraepithelial eosinophil count of ≤5 eos/hpf at Week 24; and (2) the absolute change in the subject-reported DSQ score from baseline to Week 24.

Efficacy results for Parts A and B are presented in Table 22.

**Table 22: Efficacy Results of DUPIXENT 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></th>
<th>Part B</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DUXIPXENT 300 mg QW</strong></td>
<td><strong>Placebo</strong></td>
<td><strong>Difference vs. Placebo (95% CI)</strong></td>
<td><strong>DUXIPXENT 300 mg QW</strong></td>
</tr>
<tr>
<td>N = 42</td>
<td>N = 39</td>
<td></td>
<td>N = 80</td>
</tr>
<tr>
<td><strong>Proportion of subjects achieving histological remission (peak esophageal intraepithelial eosinophil count ≤5 eos/hpf), n (%)</strong></td>
<td>25 (59.5)</td>
<td>2 (5.1)</td>
<td>57.0 (40.9, 73.1)</td>
</tr>
<tr>
<td><strong>Absolute change from baseline in DSQ score (0-84), LS mean (SE)</strong></td>
<td>-21.9 (2.5)</td>
<td>-9.6 (2.8)</td>
<td>-12.3 (-19.1, -5.5)</td>
</tr>
</tbody>
</table>

**a** Total biweekly DSQ scores range from 0 to 84; higher scores indicate greater frequency and severity of dysphagia.

**b** 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 DUPIXENT achieved histological remission (peak esophageal intraepithelial eosinophil count ≤ 6 eos/hpf) compared to placebo. Treatment with DUPIXENT 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 from Parts A and B is representative of a clinically meaningful within-subject improvement.

14.5 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 prurigo nodularis (PN), asthma, and a history of atopy (defined as having a medical history of AD, allergic rhinitis/conjunctivitis, asthma, or food allergy).

The WI-NRS is comprised of a single item, rated on a scale from 0 (“no itch”) to 10 (“worst imaginable itch”). Subjects were asked to rate the intensity of their worst pruritus (itch) over the past 24 hours using this scale. The Investigator’s Global Assessment for Prurigo Nodularis-Stage (IGA PN-S) is a scale that measures the approximate number of nodules using a 5-point scale from 0 (clear) to 4 (severe).

Efficacy was assessed with the proportion of subjects with improvement (reduction) in WI-NRS by ≥4 points, the proportion of subjects with IGA PN-S 0 or 1 (the equivalent of no itch), and the proportion of subjects who achieved a response in both WI-NRS and IGA PN-S per the criteria described above.

The 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>PRIME2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo (N=76)</td>
<td>DUPIXENT 300 mg Q2W (N=75)</td>
</tr>
<tr>
<td>Proportion of subjects with both an improvement (reduction) in WI-NRS by ≥4 points from baseline to Week 24</td>
<td>9.2%</td>
<td>38.7%</td>
</tr>
<tr>
<td>Proportion of subjects with improvement (reduction) in WI-NRS by ≥4 points from baseline at Week 24</td>
<td>18.4%</td>
<td>60.0%</td>
</tr>
<tr>
<td>Proportion of subjects with IGA PN-S 0 or 1 at Week 24</td>
<td>18.4%</td>
<td>48.0%</td>
</tr>
<tr>
<td>Proportion of subjects with improvement (reduction) in WI-NRS by ≥4 points from baseline at Week 12</td>
<td>15.8%</td>
<td>44.0%</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.

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

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)
- 300 mg of DUPIXENT in 1.14 mL solution (NDC 0024-5918-00)
- 100 mg of DUPIXENT in 0.67 mL solution (NDC 0024-5911-00)

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>
<th>100 mg/0.67 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>
<td>NDC 0024-5911-02</td>
</tr>
</tbody>
</table>

Pack of 2 pens NDC 0024-5915-02 NDC 0024-5919-02

**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)].
**What is DUPIXENT?**

DUPIXENT® (DU-pix-ent) (dupilumab) injection, for subcutaneous use

- **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.
  - 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/](https://mothertobaby.org/ongoing-study/dupixent/).

- are breastfeeding or plan to breastfeeding. 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, and 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 a needle shield or as a pre-filled pen.
  - The DUPIXENT pre-filled pen is only for use in adults and children 12 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 younger 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
  - nausea or vomiting
  - fainting, dizziness, feeling lightheaded
  - joint pain
  - skin rash
  - 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
  - chest pain
  - a feeling of pins and needles or numbness of your arms or legs

- **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 sores 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.