DUPIXENT TARGETS

UPPER AND LOWER AIRWAY INFLAMMATION

IN CRSwNP AND ASTHMA

DUPIXENT® *(dupilumab) Injection*

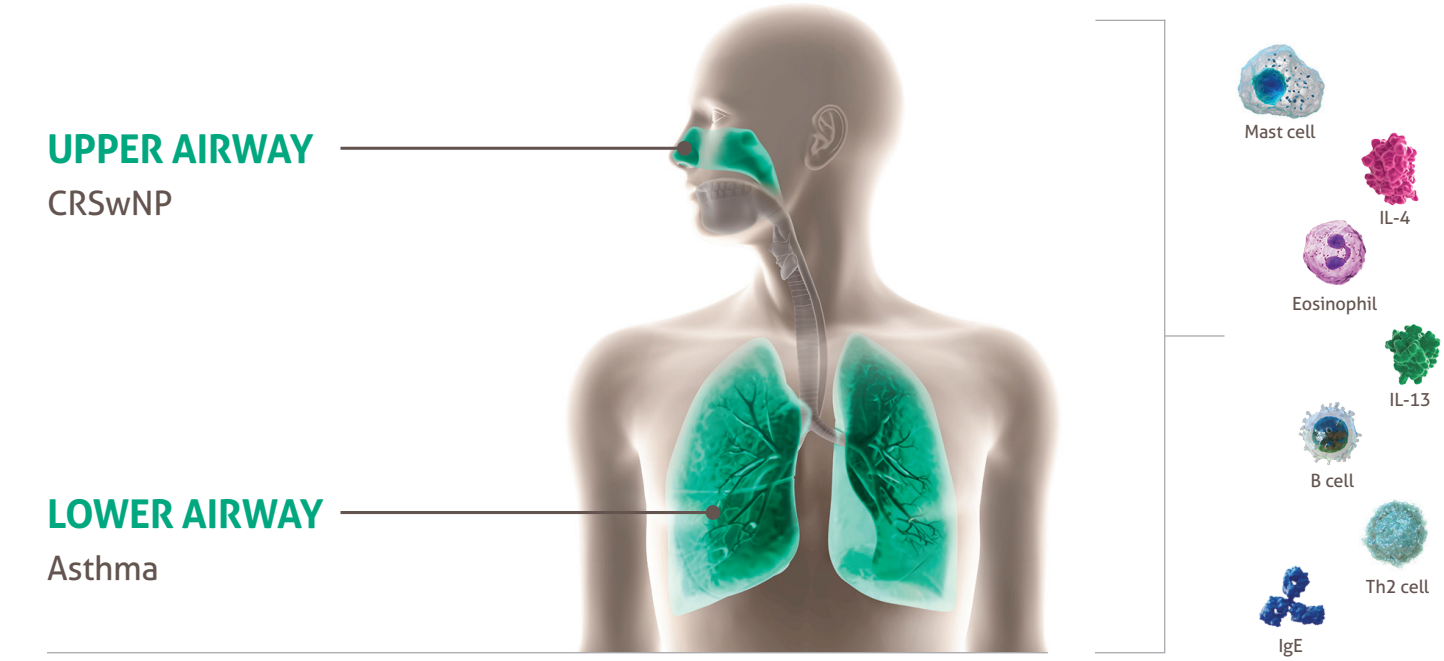
100mg · 200mg · 300mg

As add-on maintenance treatment in adult patients with inadequately controlled chronic rhinosinusitis with nasal polyposis (CRSwNP)

As add-on maintenance treatment of adult and pediatric patients (6+ years) with moderate-to-severe asthma characterized by an eosinophilic phenotype, or with OCS-dependent asthma

DUPIXENT is the first and only dual inhibitor of IL-4 and IL-13 signaling, two cytokines that contribute to underlying Type 2 inflammation in CRSwNP and asthma[1,2,a]

Type 2 inflammation plays a predominant role in CRSwNP, a disease of the nose and paranasal sinuses, which is frequently associated with comorbidities of the lower airway.[2-5]



[a] The mechanism of dupilumab action in asthma has not been established.

INDICATIONS

Asthma: DUPIXENT is indicated as an add-on maintenance treatment of adult and pediatric patients aged 6 years and older with moderate-to-severe asthma characterized by an eosinophilic phenotype or with oral corticosteroid dependent asthma. Limitation of Use: DUPIXENT is not indicated for the relief of acute bronchospasm or status asthmaticus.

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

IMPORTANT SAFETY INFORMATION

CONTRAINDICATION: DUPIXENT is contraindicated in patients with known hypersensitivity to dupilumab or any of its excipients.

OCS, oral corticosteroid.

Please see additional Important Safety Information throughout and full Prescribing Information.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hypersensitivity: Hypersensitivity reactions, including anaphylaxis, serum sickness or serum sickness-like reactions, angioedema, generalized urticaria, rash, erythema nodosum, and erythema multiforme have been reported. If a clinically significant hypersensitivity reaction occurs, institute appropriate therapy and discontinue DUPIXENT.

Conjunctivitis and Keratitis: Conjunctivitis occurred more frequently in subjects with chronic rhinosinusitis with nasal polyposis who received DUPIXENT compared to those who received placebo. There were no cases of keratitis reported in the CRSwNP development program. Among asthma subjects, the frequencies of conjunctivitis and keratitis were similar between DUPIXENT and placebo. Conjunctivitis and keratitis have been reported with DUPIXENT in postmarketing settings, with some patients reporting visual disturbances (e.g. blurred vision). 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.

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 (EGPA), 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 EGPA have been reported with DUPIXENT in adult subjects who participated in the asthma development program as well as in adult subjects with co-morbid asthma in the CRSwNP development program. A causal association between DUPIXENT and these conditions has not been established.

Acute Asthma Symptoms or Deteriorating Disease: Do not use DUPIXENT to treat acute asthma symptoms, acute exacerbations, acute bronchospasm or status asthmaticus. Patients should seek medical advice if their asthma remains uncontrolled or worsens after initiation of DUPIXENT.

Risk Associated with Abrupt Reduction of Corticosteroid Dosage: Do not discontinue systemic, topical, or inhaled corticosteroids abruptly upon initiation of 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.

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

Arthralgia: Arthralgia has been reported with use of DUPIXENT with some patients reporting gait disturbances or decreased mobility associated with joint symptoms; some cases resulted in hospitalization. Advise patients to report new onset or worsening joint symptoms. If the symptoms persist or worsen, consider rheumatological evaluation and/or discontinuation of DUPIXENT.

Parasitic (Helminth) Infections: It is unknown if DUPIXENT will influence the immune response against helminth infections. Treat patients with pre-existing helminth infections before initiating therapy with DUPIXENT. If patients become infected while receiving treatment with DUPIXENT and do not respond to anti-helminth treatment, discontinue treatment with DUPIXENT until the infection resolves. Helminth infections (5 cases of enterobiasis and 1 case of ascariasis) were reported in pediatric patients 6 to 11 years old in the pediatric asthma development program.

Vaccinations: Consider completing all age-appropriate vaccinations as recommended by current immunization guidelines prior to initiating DUPIXENT. Avoid use of live vaccines in patients treated with DUPIXENT.

ADVERSE REACTIONS:

- **Asthma:** The most common adverse reactions (incidence ≥1%) are injection site reactions, oropharyngeal pain, and eosinophilia.
- **Chronic rhinosinusitis with nasal polyposis:** The most common adverse reactions (incidence ≥1%) are injection site reactions, eosinophilia, insomnia, toothache, gastritis, arthralgia, and conjunctivitis.

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USE IN SPECIFIC POPULATIONS

- **Pregnancy:** A pregnancy exposure registry monitors pregnancy outcomes in women exposed to DUPIXENT during pregnancy. To enroll or obtain information call 1-877-311-8972 or go to https://mothertobaby.org/ongoing-study/dupixent/. 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.
- **Lactation:** There are no data on the presence of DUPIXENT 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 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.

References: 1. DUPIXENT Prescribing Information. **2.** Gandhi NA, Bennett BL, Graham NMH, Pirozzi G, Stahl N, Yancopoulos GD. Targeting key proximal drivers of type 2 inflammation in disease. *Nat Rev Drug Discov.* 2016;15(1):35-50. **3.** Stevens WW, Peters AT, Hirsch AG, et al. Clinical characteristics of patients with chronic rhinosinusitis with nasal polyps, asthma, and aspirin-exacerbated respiratory disease. *J Allergy Clin Immunol Pract.* 2017;5(4):1061-1070.e3. **4.** Langdon C, Mullol J. Nasal polyps in patients with asthma: prevalence, impact, and management challenges. *J Asthma Allergy.* 2016;9:45-53. **5.** Gelardi M, Iannuzzi L, Tafuri S, Passalacqua G, Quaranta N. Allergic and non-allergic rhinitis: relationship with nasal polyposis, asthma and family history. *Acta Otorhinolaryngol Ital.* 2014;34(1):36-41.

Please see full Prescribing Information.

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REGENERON

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