Dupixent® (dupilumab) Medicaid Core Testimonial

Timing of Response

Please see Section 14 of the package insert for the primary analyses of each indication.

Dupilumab significantly reduces itch within 2 days: In a post hoc analysis (N=1379), dupilumab 300 mg q2w significantly (*P*<0.05) lowered PPNRS scores after 2 days of treatment compared with placebo in adult patients with moderate-to-severe AD (LS mean % difference vs placebo: qw, −3.4; q2w, −4.0)[1]

Dupilumab significantly improves lung function by Week 2: Dupilumab 200 mg or 300 mg q2w significantly (*P*<0.0001) improved FEV_1 after 2 weeks of treatment compared with placebo (LS mean difference vs placebo: 200 mg, 0.14 L; 300 mg, 0.15 L) in patients aged ≥12 years with moderate-to-severe asthma (N=1902)[2]

Dupilumab improves loss of smell within 1 week: Dupilumab 300 mg q2w significantly (*P*<0.0001) improved loss of smell scores after 1 week (LS mean difference vs placebo: –0.20; score range: 0−3) and improved UPSIT scores after 2 weeks of treatment (LS mean difference vs placebo: 5.53; score range: 0−40) in adults with CRSwNP[3]

Indications, Dosage, and Administration

Please see Section 2 of the package insert for full dosage and administration information.

Indications[4]	SC Dosage and Administration[4]
Treatment of patients aged ≥6 years with moderate-to-severe AD whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable	LD Day 1 for all approved ages: double the MD MD for patients ≥18 years: 300 mg q2w MD for patients 6–17 years: • 300 mg q2w (≥60 kg) • 200 mg q2w (30 to <60 kg) • 300 mg q4w (15 to <30 kg)
Add-on maintenance treatment of patients aged ≥6 years with moderate-to-severe asthma characterized by an eosinophilic phenotype or with OCS-dependent asthma (for patients aged 6–11 years with asthma and coexisting moderate-to-severe AD, follow the recommended dosage for patients with moderate-to-severe AD, including the LD)	LD Day 1 Patients ≥12 years: double the MD Patients 6–11 years: no LD recommended MD for patients ≥12 years: • 200 or 300 mg q2w (eosinophilic phenotype) • 300 mg q2w (OCS dependence or coexisting AD) MD for patients 6–11 years: • 200 mg q2w (≥30 kg) • 100 mg q2w or 300 mg q4w (15 to <30 kg)
Add-on maintenance treatment in adult patients with inadequately controlled CRSwNP	MD for patients ≥18 years: 300 mg q2w

ICER 2021 AD Report

Dupilumab is associated with favorable long-term cost effectiveness compared with JAK inhibitors and tralokinumab in adults with moderate-to-severe AD[5]

- In an indirect treatment comparison, ICER concluded that there was insufficient evidence to support the superiority of abrocitinib and upadacitinib over dupilumab 300 mg q2w, in terms of net health benefit in adults with moderate-to-severe AD, and that incremental cost-effectiveness ratios favored dupilumab
  - The net health benefit of baricitinib and tralokinumab was found to be comparable or inferior to dupilumab
  - Compared with dupilumab, baricitinib and tralokinumab were less costly and less effective over a 5-year treatment period, while abrocitinib and upadacitinib were not cost-effective versus dupilumab
- Concerns about the lack of long-term safety data for dupilumab, as noted in ICER's 2017 report, have been alleviated over time on the basis of published data and widespread use in clinical practice

New Clinical Data

Dupilumab post hoc analysis: In LIBERTY ASTHMA QUEST, dupilumab 200 and 300 mg q2w significantly reduced exacerbation rates and improved lung function in patients with uncontrolled, moderate-to-severe allergic asthma[6]

- Allergic asthma (n=1083) was defined as total serum IgE ≥30 IU/mL and ≥1 positive allergen-specific IgE value (≥0.35 kU/L)
- In the allergic asthma subgroup, dupilumab was associated with greater reductions in exacerbations rates at Week 52 (% difference vs placebo: dupilumab 200 mg, –36.9%; dupilumab 300 mg, –45.5; both *P*<0.01) and improvements in FEV_1 at Week 12 (LS mean difference vs placebo: dupilumab 200 mg, 0.13 L; dupilumab 300 mg, 0.16 L; both *P*<0.001) compared with placebo

According to Peters et al, a CRSwNP indirect treatment comparison, dupilumab improved key CRSwNP outcomes compared with omalizumab[7]

- Dupilumab 300 mg q2w was associated with significant improvements in NPS, NC score, and sense of smell at Week 24 compared with omalizumab q2w–q4w in adults with severe CRSwNP[7]
  - Mean difference in NPS of −1.04 (95% CI, −1.63 to −0.44) was observed in dupilumab-treated versus omalizumab-treated patients
  - Mean difference in NC scores between the dupilumab and omalizumab groups was −0.35 (−0.60 to −0.11)
  - Mean differences in loss of smell and UPSIT scores between the dupilumab and omalizumab groups were −0.66 (−0.90 to −0.42) and 6.70 (4.67 to 8.73), respectively
  - Dupilumab demonstrated significantly greater improvements in all key outcome measures versus omalizumab except for the SNOT-22 score, which showed greater numerical improvement with dupilumab versus omalizumab without being statistically significant (mean difference [95% CI]: –3.47 [–9.07 to 2.12])

There are no head-to-head data comparing omalizumab and dupilumab; indirect treatment comparisons have inherent limitations, which are fully addressed in the manuscript.

Dupilumab is OCS and surgery sparing in adults with CRSwNP: In a pooled analysis of SINUS-24 and SINUS-52 (N=276), dupilumab 300 mg q2w and q2w–q4w significantly reduced OCS use and/or need for sinonasal surgery[8]

- Dupilumab significantly reduced the need for SCS by 73.9% versus placebo over the 52-week treatment period (HR [95% CI]: 0.261 [0.179 to 0.379]; *P*<0.0001)
- Dupilumab significantly reduced the number of patients requiring NP surgery by 82.6% versus placebo over the 52-week treatment period (HR [95% CI]: 0.174 [0.066–0.462]; *P*=0.0005)

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Coexisting Type 2 Inflammatory Disease

Dupilumab improves AD, asthma, and CRSwNP symptoms in adults with moderate-to-severe AD with coexisting asthma and CRSwNP

- In a pooled analysis of LIBERTY AD SOLO 1, SOLO 2, CHRONOS, and CAFÉ (N=2444), dupilumab 300 mg qw or q2w provided significant and clinically meaningful improvements in AD severity and itch, asthma control, and sinonasal symptoms in adults with moderate-to-severe AD with coexisting asthma and CRSwNP[9]
  - Significantly (*P*<0.0001) more patients treated with dupilumab achieved ≥75% improvements from baseline EASI scores (dupilumab qw: 51.0%; dupilumab q2w: 52.6%) versus placebo (17.5%) at Week 16; additionally, dupilumab significantly (*P*<0.0001) lowered Week 16 PPNRS scores versus placebo (LS mean change from baseline PPNRS score: dupilumab qw, 3.75; dupilumab q2w, 3.44; placebo, 1.74)
  - Significantly more patients treated with dupilumab versus placebo achieved clinically meaningful improvements in 5-item ACQ (dupilumab qw: 47.1%; dupilumab q2w: 31.6%, placebo: 21.9%; *P*<0.001 and *P*<0.05 vs placebo, respectively) and SNOT-22 (dupilumab qw: 43.1%; dupilumab q2w: 33.7%, placebo: 14.9%; *P*<0.001 and *P*<0.001 vs placebo, respectively) scores at Week 16

Dupilumab improves asthma symptoms and QOL in adults with CRSwNP and coexisting asthma

- In a pooled analysis of SINUS-24 and SINUS-52, dupilumab 300 mg q2w significantly improved pulmonary function and QOL in adults with coexisting CRSwNP and asthma[10]
  - Dupilumab significantly (*P*<0.001) improved NPS, NC, LMK-CT, and SNOT-22 scores versus placebo at Week 24 (refer to the full manuscript for additional details)
  - Dupilumab significantly (*P*<0.001) improved FEV_1 (LS mean difference [95% CI]: 0.21 L [0.13–0.29]) and 6-item ACQ scores (LS mean difference [95% CI]: –0.82 [–0.98 to –0.67]) versus placebo at Week 24

AD 2017 Consensus Statement

The 3AD Steering Committee[a] concluded the following:

> *"dupilumab has shown strong efficacy and safety for treatment of moderate-to-severe AD in adults. Considering the safety profiles of conventional systemic therapies, which are not FDA-approved for AD treatment, it is recommended that dupilumab be used as a first-line systemic treatment in adults with moderate-to-severe AD who are uncontrolled with topical therapies"*[11]

- Many patients with moderate-to-severe AD are not receiving systemic therapy because of a lack of approved, safe, and effective therapies and the significant burden of adverse events with off-label use of currently available immunosuppressants[11]

Asthma 2021 Guidelines

The GINA 2021 Report concluded that

> *"dupilumab is recommended for the treatment of severe Type 2 eosinophilic asthma in patients who require maintenance oral corticosteroids, or patients who experienced exacerbations in the last year and have either blood eosinophil levels ≥150 cells/μL or FeNO levels ≥25 ppb"*[12]

- Elevated blood eosinophils or FeNO are predictive of a good response to dupilumab[12]
- Dupilumab was also noted to be indicated for the treatment of patients with moderate-to-severe AD or CRSwNP[12]

Dupilumab Is Not an Immunosuppressant

- Dupilumab is not classified as an immunosuppressant by the FDA and WHO[4,13]
  - Dupilumab is an interleukin-4 receptor alpha antagonist[4]
- No meaningful changes in routine laboratory parameters were found in adults with moderate-to-severe AD treated with dupilumab[14]
- Studies have supported that patients taking dupilumab have no increased risk of infection[15–17]
  - Serious or severe infections, nonherpetic skin infections, and clinically concerning herpes viral infections (eczema herpeticum and herpes zoster) were significantly (*P*=0.02, *P*<0.001, and *P*=0.004, respectively) lower with dupilumab versus placebo[15]
  - URTIs were significantly (nominal *P*<0.01) less likely to occur in dupilumab-treated patients aged ≥12 years with moderate-to-severe asthma versus placebo[16]
  - URTIs were significantly (*P*≤0.01) less likely to occur in adults with CRSwNP treated with dupilumab compared with placebo[17]

Safety

- AD: Most common adverse reactions (incidence ≥1%) are injection site reactions, conjunctivitis, blepharitis, oral herpes, keratitis, eye pruritus, other herpes simplex virus infection, and dry eye[4]
- Asthma: Most common adverse reactions (incidence ≥1%) are injection site reactions, oropharyngeal pain, and eosinophilia[4]
- CRSwNP: Most common adverse reactions (incidence ≥1%) are injection site reactions, eosinophilia, insomnia, toothache, gastritis, arthralgia, and conjunctivitis[4]
- Hypersensitivity reactions (urticaria, rash, erythema nodosum, erythema multiforme, anaphylaxis, and serum sickness) have occurred after administration of dupilumab[4]
- The incidences of treatment discontinuation due to adverse events were as low as or lower with dupilumab compared with placebo across all indications[4]
- For additional important safety information, please see "Dupilumab package insert" linked below

Additional Information

- Dupilumab package insert
- Dupilumab patient information
- References

[a]Sanofi Genzyme and Regeneron provided funding for the 3AD program but had no influence on the development of the recommendations.

5-item ACQ score range[9]: 0–6; 6-item ACQ score range[10]: 0–6; EASI score range[1]: 0–72; LMK-CT score range[10]: 0–24; loss of smell score range[3]: 0–3; NC score range[10]: 0–3; NPS score range[10]: 0–8; PPNRS score range[1]: 0–10; SNOT-22 score range[9]: 0–110; UPSIT score range[3]: 0–40.

ACQ, Asthma Control Questionnaire; AD, atopic dermatitis; CRSwNP, chronic rhinosinusitis with nasal polyps; EASI, Eczema Area and Severity Index; FDA, Food and Drug Administration; FeNO, fractional exhaled nitric oxide; FEV_1, forced expiratory volume in 1 second; GINA, Global Initiative for Asthma; HR, hazard ratio; ICER, Institute for Clinical and Economic Review; Ig, immunoglobulin; JAK, Janus kinase; LD, loading dose; LMK-CT, Lund-MacKay computed tomography; LS, least squares; MD, maintenance dose; NC, nasal congestion; NP, nasal polyps; NPS, nasal polyp score; OCS, oral corticosteroids; ppb, parts per billion; PPNRS, peak pruritus numerical rating scale; q2w, every 2 weeks; q4w, every 4 weeks; QOL, quality of life; qw, every week; SC, subcutaneous; SNOT-22, 22-item Sinonasal Outcomes Test; UPSIT, University of Pennsylvania Smell Identification Test; URTI, upper respiratory tract infection; WHO, World Health Organization.