Dupilumab in DUPIXENT in Chronic Spontaneous Urticaria (CSU)
National Drug Mini-Monograph

January 2026

VA Pharmacy Benefits Management Services and National Formulary Committee

The purpose of VA PBM Services drug monographs is to provide a focused drug review for making formulary decisions. The Product Information or other resources should be consulted for detailed and most current drug information.

Abbreviations: AC, active-controlled; ADE, adverse drug event; CO, crossover; DB, double-blind; GRADE, Grading of Recommendations, Assessment, Development, and Evaluation; H1 AH, antihistamines; HSS7, mean weekly hive severity score; ISS7, mean weekly itch severity score; MC, multicenter; MN, multinational; OCS, oral corticosteroids; Oma, omalizumab; PBO, placebo; PC, placebo-controlled; R, randomized; RCT, randomized clinical trial; TEAE, treatment emergent adverse event; UAS7, urticaria activity score; UCT, urticaria control test

FDA PRESCRIBING INFORMATION[1]	
Description / MOA	Human monoclonal IgG4 antibody that inhibits interleukin-4 (IL-4) and interleukin-13 (IL-13) signaling by binding to the IL-4α subunit.
Indication Under Review	Treatment of chronic spontaneous urticaria (CSU) in adults (and pediatrics patients $\geq$ 12 years) who remain symptomatic despite treatment with H_1 antihistamines.
Dosage Regimen	Initial dose=600 mg Maintenance dose=300 mg every 2 weeks
Dosage Forms Under Review	*Injection: single dose prefilled syringe with needle shield and prefilled pen* *300 mg/2 mL*

EFFICACY CONSIDERATIONS	
Trial	**LIBERTY-CSU CUPID (A and B; 2 Phase 3 trials)**
Design	R, DB, MC, PC x 24 weeks (2-4-week screening; 24-week treatment; 12-week posttreatment)
Population	Study A: Patients with CSU diagnosis > 6 months and remained symptomatic despite H1 AH at approved doses or higher. Study B: Patients with CSU diagnosis with omalizumab-intolerant or those with an incomplete response. Incomplete response was defined as: Oma ≥ 300 mg every 4 weeks for ≥ 3 months (3 injection minimum) who had an inadequate response or intolerance and confirmed by and stopped by study investigator. Included: Patients were required to have itch and hives for > 6 weeks prior to screening; weekly UAS7 ≥ 16 (range 0-42) and ISS7 ≥ 8 (range 0-21) within 7 days of being randomized. *In both studies, H1 AH were continued and allowed to be titrated up to 4x the usual daily dose. Rescue with oral corticosteroids was permitted.* Excluded: Patients with inducible urticaria, diseases other than urticaria associated with hives or angioedema and active atopic dermatitis or other skin condition that could interfere with outcome assessments.
Intervention	Dupilumab 600 mg loading dose followed by 300 mg every 2 weeks x 24 weeks H1 AH
Comparator	PBO every 2 weeks x 24 weeks
Key Baseline Characteristics	Mean Age: 41 years (Study A); 47 years (Study B) ISS7: 15.9 (Study A): 16 (Study B) (Scores range from 0-21, higher scores indicate more symptoms) UAS7: 31.3 (Study A); 31.5 (Study B) (Scores range from 0-42, 16-27=moderate; ≥ 28=severe symptoms) UAS7 ≥ 28 (severe symptoms): 70.3% (Study A); 69.4% (Study B) Angioedema: 44.9% (Study A); 49.1% (Study B) Standard dose H1 AH: 52.2% (Study A); 36.4% (Study B) 4-fold dose H1 AH: 16.7% (Study A); 25.2% (Study B) Incomplete OMA responder: 96.3%; OMA intolerant: 3.7% (Study B)
Outcome Measures	Primary: change from baseline in ISS7 at 24 weeks Secondary: change from baseline in UAS7 at 24 weeks; proportion of patients with UAS7 ≤ 6, =0 and improvement in ISS7 ≥ 5 points from baseline; change from baseline in weekly hives severity score (HSS7) and urticaria control test (UCT) at 24 weeks. *(European Medicines Agency used change from baseline in UAS7 as primary and ISS7 as secondary endpoints)*

Results *(change from baseline to 24 weeks)*

LIBERTY-CSU CUPID (Studies A and B)

Outcome	Dupilumab (N=70-A)	PBO (N=68-A)	Dupilumab (N=54-B)	PBO (N=54-B)	Comments
Primary: Change in ISS7* (MCID 4.5-5)	-10.2 vs. PBO: -4.2; p=0.0005	-6	-7.7 vs. PBO: -2.9	-4.8	Primary endpoint in non-EU countries
Change in UAS7* (MCID 9.5-11)	-20.5 vs. PBO: -8.5; p=0.0003	-12	-14.4 vs. PBO: -5.8; p=0.039	-8.5	Primary endpoint in EU countries. Difference is statistically significant in EU but not in non-EU countries
Change in HSS7	-10.3 vs. PBO: -4.4; p=0003	-5.9	-6.6 vs. PBO: -3; p=0.397	-3.6	
% UAS7 ≤ 6 and =0	45.7% (1.3-6.2); p=0.008 and 31.4% (1.2-7.2); p=0.02 vs. PBO	23.5% and 13.2%	24.1% (0.6-6.2); p=0.31 and 13% (0.3-5.2); p=0.84	18.5% and 9.3%	
Change in ISS7 ≥ 5 pts	72.9% vs. PBO (1.6-7.3); p=0.0014	42.6%	59.3% vs. PBO (0.8-4.7); p=0.12	38.9%	
Change in UCT	7.7 vs. PBO: 2.8 (1.3-4.4); nominal p value 0.0004	4.9	5.3 vs. PBO (0-3.9); p=0.05	3.5	

Sources: [2] MCID=minimally important clinical difference-values are generally accepted based upon findings from clinical trials.

Rescue medications included increased doses of H1 AH (up to 4 x usual daily dose) and short course of OCS (no statistics applied, small numbers in both groups and studies e.g., 2-5 courses of OCS).

In Study B, prespecified efficacy criteria for futility were reviewed during a planned interim analysis which met criteria for futility. However, the study continued until study completion. All p-values are nominal (not adjusted for multiplicity) except UAS7, which was statistically different vs. PBO, but only in EU countries.

Weekly itch severity score (ISS7): Daily scores summed over 7-days; scores range 0-21; higher scores indicate more severe symptoms, no validated cut-offs for severity of disease; MCID=4.5-5 pts

Weekly hives severity score (HSS7): Daily scores summed over 7 days; scores range 0-21; daily scores: 0=no hives, 1=mild (<20 hives), 2=moderate (20-50 hives), 3=intense (>50 hives or large confluence area); MCID ≥ 5 pts.

Mean weekly urticaria activity score (UAS7): range 0-42; 0-6 = well controlled disease; 7-15 mild; 16-27 moderate; ≥ 28 severe disease; MCID=9.5-11 pts***. Daily ISS7 and HSS7 scores over a 7-day period are added to get UAS7 score.***

Urticaria control test (UCT): range 0-16. Measures disease control; range 0-16; score of ≥ 12 represents well controlled disease; MCID 3 pts (2 if using UCT7)

Authors' Conclusions

Dupilumab significantly improved urticarial disease activity by reducing severity of itch and hives in patients with CSU who remain symptomatic despite use of H1 AH and naïve to treatment with omalizumab (IgE monoclonal antibody-approved for CSU) (Study A). In study B, patients who were intolerant of or had an incomplete response to at least 3 months of treatment with omalizumab did not show a statistically significant response vs. placebo. During a planned interim analysis, prespecified criteria for futility were met. The authors theorized that the study may have been underpowered to demonstrate a smaller treatment benefit of dupilumab is this group of patients.

SAFETY CONSIDERATIONS	
Boxed Warnings	None
Contraindications	Known hypersensitivity to dupilumab or any excipients
Other Warnings	Hypersensitivity; conjunctivitis and keratitis (report new eye symptoms to provider); eosinophilic conditions (especially upon reducing oral corticosteroid dose); steroid withdrawal (do not abruptly discontinue oral, topical or inhaled corticosteroids upon initiation. If needed, gradually decrease steroids); psoriasis (new onset report to provider); arthralgia and psoriatic arthritis (report new onset joint symptoms to provider); parasitic (Helminth) infections (treat preexisting infections before initiating treatment); vaccines (avoid use of live vaccines).
Top 5 AEs	Injection site reactions, regardless of indication. Refer to prescribing information for ADEs reported in clinical trials for specific conditions.
Drug Interactions	None
Pregnancy	Case reports and case series in pregnant women have not identified a dupilumab-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. There is a pregnancy registry monitoring outcomes in pregnant women exposed to dupilumab during pregnancy.
Lactation	Unknown. The benefits of breast feeding should be considered along with the mother's clinical need for dupilumab, any potential ADEs on the breastfed child from dupilumab or from the mother's underlying condition.
Trial Safety Results	Similar TEAE (57.3% Dup vs. 56.6% PBO) and withdrawal due to ADEs (1.6% Dup vs. 3.3% PBO) observed in LIBERTY-CUPID Studies A and B.

OTHER CONSIDERATIONS	
FDA Review	N/A
ICER Review	N/A
NICE Review	Planned review suspended in 2023 since the company was not prepared to submit the CSU indication for approval.
Other	The phase 3 LIBERTY-CSU CUPID Study C has not been published in a peer-reviewed journal. However, Regeneron and Sanofi announced results of the study in September 2024 which reportedly confirm the results reported from Study A in a population with CSU who remain symptomatic despite use of H1 AH and who have not received omalizumab. Study C enrolled 151 children and adults (n=74 dupilumab; n=77 placebo) who were treated for 24 weeks. The press release noted "complete response" in 30% of dup vs. 18% placebo recipients. A "complete response" was noted in a similar proportion of patients based upon achieving UAS7 equal to zero in Study A. Itch was reported to decrease by 8.64 points in dup vs. 6.10 in placebo (p=0.02) both groups reaching MCID of 4.5-5 points. For urticaria activity severity (UAS7-measuring hives and itch), dup improved the score by 15.86 vs. 11.21 for placebo (p=0.02). Both groups reaching MCID of 9.5-11 for UAS7.[3]

THERAPEUTIC ALTERNATIVES AND THEIR PLACE IN THERAPY

DRUG	VANF	CFU	FDA	GUIDELINES[4-5]
Omalizumab	PA-F	Yes-CSU or CIU	Approved for patients who remain symptomatic despite use of H1 AH (2014)	2nd line for patients remaining symptomatic on H1 AH (up to 4x daily dose)
Cyclosporine	F	No	Off-Label for refractory CSU	3rd line for patients remaining symptomatic on H1 AH (up to 4x daily dose) + omalizumab
Remibrutinib	TBD	Pending	Approved for patients who remain symptomatic despite use of H1 AH (September 2025)	SR concludes that Oma and Remi are most effective, but safety remains less certain for Remi.[5] Dup impact on QOL and angioedema activity is uncertain.

POTENTIAL PLACE IN THERAPY OF ——

1. In patients with CSU who remain symptomatic despite taking H1 AH to up to 4 times the usual daily dose. Indirect evidence supports a greater effect of omalizumab in patients with CSU. Patients who do not have an adequate response to omalizumab are unlikely to have a greater response to dupilumab, based upon the LIBERTY-CSU CUPID B study. LIBERTY-CSU CUPID B study was small and additional evidence is needed to determine whether patients who do not have a sufficient response to omalizumab will have greater benefit when switching to dupilumab.
2. Maximum doses of H1 AH should be continued in combination with second line therapies.
3. Low dose cyclosporine may be considered as a third line agent in patients with more refractory symptoms/disease.
4. Therapy can be stepped down by reducing doses or extending dosing intervals when the urticaria control test (UCT) is equal to 16.

Revisions: N/A
Original: January 2026.
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References

1 DUPIXENT (Dupilumab) injection. [prescribing information online]. Tarrytown, NY; Regeneron Pharmaceuticals, Inc/Sanofi-Aventis US, LLC. June 2025. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761055s070lbl.pdf (Accessed October 2025)

2 Maurer M, Casale TB, Saini SS, et al. Dupilumab in Patients with Chronic Spontaneous Urticaria (LIBERTY-CSU CUPID): Two, Randomized, Double-Blind, Placebo-Controlled, Phase 3 Trials. J Allergy Clin Immunol 2024;154:184-194.

3 Dupixent® (dupilumab) Phase 3 Trial Confirms Significant Improvements in Itch and Hives for Patients with Chronic Spontaneous Urticaria (CSU) September 11, 2024. https://investor.regeneron.com/news-releases/news-release-details/dupixentr-dupilumab-phase-3-trial-confirms-significant (Accessed October 2025)

4 Torsten Zuberbier, Amir Hamzah Abdul Latiff, Mohamed Abuzakouk, et al. The International EAACI/GA²LEN/EuroGuiDerm/APAAACI Guideline for the Definition, Classification, Diagnosis, and Management of Urticaria. Allergy 2022;77:734-766.

5 Chu AWL, Oykhman P, Chu X, et al. Comparative Efficacy and Safety of Biologics and Systemic Immunomodulatory Treatments for Chronic Urticaria: Systemat Review and Network Meta-Analysis. J Allergy Clin Immunol 2025;156:1008-1023. *(Systematic search as part of the update of the American Academy of Allergy, Asthma and Immunology (AAAAI), the American College of Allergy, Asthma and Immunology (ACAAI) and the Joint Task Force on Practice Parameters (JTFPP) Guidelines for Chronic Urticaria)*