Dupilumab (DUPIXENT) in Bullous Pemphigoid
National Drug Mini-Monograph

November 2025

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: AE, adverse event; AZP, azathioprine; BP, bullous pemphigoid; CIU, chronic idiopathic urticaria; CS, corticosteroid(s); CSU, chronic spontaneous urticaria; DAS, disease activity score; DB, double-blind; GRADE, Grading of Recommendations, Assessment, Development, and Evaluation; ID, insufficient data; IMPDH, inosine monophosphate dehydrogenase; IST, immunosuppressive therapy (e.g., methotrexate, azathioprine, mycophenolate); MAB, monoclonal antibody; MC, multicenter; MMF, mycophenolate mofetil; MN, multinational; OCS, oral corticosteroid(s); PBO, placebo; PC, placebo-controlled; PP-NRS–4, Peak Pruritus Numerical Rating Scale score reduction of at least 4 points; Q, GRADE quality of evidence; RCT, randomized clinical trial; SustRem, sustained remission; TCS, topical corticosteroid(s)

FDA PRESCRIBING INFORMATION	
Description / MOA[1]	Monoclonal IgG4 antibody to interleukin (IL)-4 receptor-alpha with IL-4 and -13 inhibitory effects
Indication Under Review	Treatment of adults with bullous pemphigoid (BP)
Dosage Regimen	600 mg SC once, then 300 mg SC every 2 weeks Use in combination with a tapering course of oral corticosteroids (OCS). Once disease control has occurred, gradually taper OCS after which continue dupilumab as monotherapy. In case of relapse, corticosteroids (CS) may be added if medically advisable.
Dosage Forms Under Review	Prefilled syringe and pen: 300 mg/2 mL
Pretreatment Procedures	None
Treatment Monitoring	No laboratory monitoring is required. Monitor for keratoconjunctivitis.

EFFICACY CONSIDERATIONS	
Trial	**Unpublished LIBERTY-BP ADEPT**[2]
Design	52-week phase 2/3 MN DB PC RCT *Primary Endpoint*: Rate of sustained remission (SustRem) at Week 36. SustRem was defined as complete remission and off OCS no later than Week 16, absence of disease relapse from OCS discontinuation to Week 36, and absence of rescue therapy during the 36-week DB treatment period. *QoL Evaluation:* Autoimmune Bullous Disease Quality of Life (ABQOL) questionnaire (validated).
Population	106 patients with moderate–severe, histopathologically, immunopathologically, and serologically confirmed diagnosis of BP; Bullous Pemphigoid Disease Area Index (BPDAI) activity score ≥ 24 (scale, 0–360 with scores ≤ 19 defining mild, 20–56 moderate, and ≥ 57 severe disease[3]) and weekly average Peak Pruritus NRS (PP-NRS) score ≥ 4 (scale, 0–10 with scores < 3 defining mild, ≥ 3 to < 7 moderate, ≥ 7 to < 9 severe, and ≥ 9 very severe pruritus). *Baseline Characteristics:* Mean age 71.3 yrs; 47% male; 68% White; 63% prior systemic CS use for BP; PP-NRS 7.5
Interventions	Dupilumab 600 mg SC then 300 mg Q2W Placebo
Co-therapy	Tapering OCS (prednisone/prednisolone 0.5 or 0.75 mg/kg/d; tapered after disease controlled for 2 weeks with goal of discontinuing no later than Week 16)
Rescue Therapy	Topical corticosteroids (TCS), OCS, nonsteroidal immunosuppressive therapy (IST), or biologic immunomodulators

Results

Efficacy Results at Week 36

Outcome	DUP + OCS	PBO + OCS	RR (95% CI)	Diff or AAE (95% CI)	NNT (95% CI)	Q
SustRem, n/N (%)	10/53 (18.3)	3/53 (6.1)	3.3 (0.97, 11.4)	12.2 (–0.8, 26.1)	8 (4, 103)	ID
PP-NRS–4, n/N (%)	20/53 (38.3)	6/53 (10.5)	3.3 (1.45, 7.64)	27.8 (11.6, 43.4)	4 (3, 10)	ID

Sources: 1

Other Results (DUP + OCS vs PBO + OCS):

- Received Rescue Therapy: 53% vs 79%
- Median Cumulative OCS Dose (min, max): 2.8 g (1.2, 22.7) vs 4.1 g (1.5, 23.3)

Limitations

Unpublished study.

No evaluation of the clinical effects of reduced OCS use (e.g., CS-related adverse events).

ABQOL results were not reported.

PBM Comments

- Numerical improvement in SustRem at Week 36 with a wide confidence interval that includes a treatment difference of –0.8 (potentially ineffective, potentially clinically unimportant effect) to a moderate effect (26.1). Results were limited by a small study size.
- The clearer benefit, based on a 95% CI > 0, was a moderate effect in achievement of a clinically important change in PP-NRS (i.e., PP-NRS–4).

SAFETY CONSIDERATIONS

Top 5 AEs in BP	Arthralgia, conjunctivitis, blurred vision, herpes viral infections, keratitis

OTHER CONSIDERATIONS

FDA Review	Not available
ICER Review	Not available
NICE Review	In development

THERAPEUTIC ALTERNATIVES WITH SIMILAR PLACE IN THERAPY

DRUG	VANF	CFU	FDA	EADV GUIDELINES[4]	CONSIDERATIONS
Dupilumab (DUP) IL-4/13 inhibitor	No	AD, CRSwNP, EoE, COPD TBD for BP	Use in combination with tapering OCS. Once disease is controlled, gradually taper OCS after which DUP may be continued as monotherapy.	Consider for BP resistant to combined TCS and OCS	The only agent FDA-approved for BP and the only biologic showing benefit for BP in a RCT. Different MOA. Favorable safety profile; nonimmunosuppressant (advantageous in the typical older BP patient population with comorbidities). EADV guidelines preceded publication of ADEPT.
Omalizumab (OMZ) Anti-IgE MAB	PA-F	Asthma CIU/CSU	Off label for BP	Consider for BP resistant to combined TCS and OCS	Lacks RCT in BP. Nonimmunosuppressant.
Rituximab (RTX) B cell anti-CD20 MAB	No	No	Off label for BP	Consider for BP resistant to combined TCS and OCS	Lacks RCT in BP. In a systematic review of non-RCTs, RTX was associated with higher rates of recurrence, adverse events, and mortality than DUP and OMZ.[5]

DRUG	VANF	CFU	FDA	EADV GUIDELINES[4]	CONSIDERATIONS
Globulin, Immune Inj/IV Immunoglobulins (IVIG) Immunomodulator, antiinflammatory	Yes	No	Off label for BP	Consider for BP resistant to combined TCS and OCS	One PC RCT (Bullous Pemphigoid Study). IVIG showed NSD vs PBO in the Disease Activity Score (DAS) primary endpoint in 56 Japanese patients refractory to OCS.[6] Post hoc analysis showed a significant difference using DAS on Day 1 as a covariate. Subgroup analysis showed an early significant treatment difference in severe BP (DAS ≥ 40). NSD in AEs. Dose of human IgG: 400 mg/kg/d for 5 consecutive days. Nonimmunosuppressant; considered useful in severe cases or when rapid onset is needed. Infusion reactions
Methotrexate Folate antagonist; immunosuppressant; antiinflammatory	Yes	No*	Off label for BP	May be recommended for contraindications or resistance to CS	Lacks RCT in BP. Once-WEEKLY dosing. Administer with folic acid to reduce adverse effects.
Azathioprine (AZP) Inhibitor of DNA replication, purine synthesis, and B- and T-cells	Yes	No	Off label for BP	May be recommended for contraindications or resistance to CS	Two active-controlled RCTs in BP (lacks PC RCT): In a MC OL RCT in Germany (N = 73), AZP + OCS and MMF + OCS were similar in achieving complete remission and in cumulative OCS dose. AZP had a numerically higher rate of grade 3–4 AEs and statistically higher rate of liver enzyme elevations than MMF.[7] In a MC OL RCT, AZP + OCS (N = 36) was similar to plasma exchange + OCS (N = 31) and to OCS (prednisolone) alone (N = 31) in rates of complete remission at 28 days and 6 months and in mortality rates at 6 months.[8] AZP + OCS was associated with major adverse effects (e.g., cytopenia, hepatitis) in 25% of patients vs 10% on OCS + plasma exchange and 16% of patients on OCS alone. Deaths occurred in 17%, 10%, and 16% of patients, respectively. *Neither AZP nor plasma exchange provided additional benefits over OCS.*
Mycophenolate Mofetil (MMF) Inhibitor of IMPDH and T- and B-cell proliferation	Yes	No	Off label for BP	May be recommended for contraindications or resistance to CS	One active-controlled RCT in BP: As described under AZP, relative to AZP + OCS, MMF + OCS was similar in efficacy and cumulative OCS dose and had better safety.[7] *Lack of evidence that MMF provides additional benefits over OCS.*

* See PBM Sharepoint > Clinical Guidance > Clinical recommendations > *Methotrexate Contraindications and Risk Factors for Serious Adverse Events in Inflammatory Disorders.*

POTENTIAL PLACE IN THERAPY OF DUPILUMAB IN BP	
Epidemiology	1. Bullous pemphigoid is a relatively uncommon disease, affecting slightly more females than males and mostly older adults ≥ 60 years of age. Most estimates of the incidence of bullous pemphigoid come from European studies that showed 4–22 cases per million individuals per year carry the diagnosis.[9] The most recent published study in the US analyzed data (1960 through 2009) from Olmsted County, Minnesota and estimated that the incidence of bullous pemphigoid was 2.4 per 100,000 person-years (95% CI 1.9, 2.9).[10] The incidence may be increasing for various reasons including population aging and increasing use of drugs associated with BP.[9] 2. Based on VHA prescription-diagnosis data from 7/1/2024 to 6/30/2025, 2,589 patients had a diagnosis of bullous pemphigoid. Of seven selected systemic therapies likely to be used for corticosteroid-sparing therapy in patients with moderate to severe or refractory BP (azathioprine, dupilumab, IV immunoglobins/globulin immune injection, methotrexate, mycophenolate mofetil, omalizumab, and rituximab), the three agents most commonly used in VHA patients with a diagnosis of bullous pemphigoid were dupilumab (n = 335) followed by mycophenolate mofetil (n = 153) and methotrexate (n = 77).
1L in combination with tapering OCS	1. The ADEPT trial showed promising but inconclusive benefits from dupilumab therapy in achieving sustained remission after tapering off OCS in mostly elderly white females who had moderate to severe bullous pemphigoid with moderate to very severe pruritus and had or had not received prior OCS. In a minority of patients (18.3%), it sustained remission after tapering off of OCS, eliminating the need for long-term concomitant OCS or rescue OCS therapy. However, the treatment difference from placebo (6.1%) was not statistically significant for this efficacy measure. Dupilumab showed small to moderate benefits in achieving clinically important reductions in peak pruritus numerical rating scale scores (i.e., PP-NRS–4, where reductions of ≥ 2–4 points indicate clinically meaningful improvements). No data were available for effects on quality of life. The study population did not represent the predominantly male VHA patient population but there is no compelling reason to avoid use of dupilumab in VHA patients with bullous pemphigoid. 2. The main advantages of dupilumab are a better, nonimmunosuppressant safety profile relative to other systemic immunosuppressant treatment alternatives. Lack of immunosuppression is an advantage since patients with bullous pemphigoid are typically older with comorbidities. The efficacy and safety of dupilumab are supported by a placebo-controlled RCT. Alternative treatments lack RCTs or PC RCTs, or showed no significant benefit in a PC RCT (e.g., IVIG). 3. Dupilumab is the first medication FDA-approved for bullous pemphigoid and is a potential first-line (1L) treatment in combination with a tapering course of OCS in patients who have moderate to severe BP or need systemic therapy.

DRUG COSTS				
Drug	**Dosage**	**Product**	**Pkg Price ($)**	**Price for 52 Wks ($)**
Dupilumab	600 mg then 300 mg Q2W	DUPIXENT PEN 300 mg/2 mL #2	2214.38	28,787

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References

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