Iowa Medicaid
IOWA HHS

PDL DRUG REVIEW

Proprietary Name: Bimzelx®
Common Name: bimekizumab-bkzx
PDL Category: Anti-Inflammatories Non-NSAID

Comparable Products	Preferred Drug List Status
Cosentyx	Non-Preferred with Conditions
Siliq	Non-Preferred with Conditions
Taltz	Preferred with Conditions

Pharmacology/Usage: Bimekizumab-bkzx, the active ingredient of Bimzelx®, is an interleukin (IL)-17 A and F antagonist. It is a recombinant humanized immunoglobulin G1 (IgG1) monoclonal antibody with two identical antigen binding regions that selectively bind to human IL-17A, IL-17F, and interleukin 17-AF cytokines, and inhibits their interaction with the IL-17 receptor complex. IL-17A and IL-17F are naturally occurring cytokines that are involved in normal inflammatory and immune responses. Bimekizumab-bkzx inhibits the release of proinflammatory cytokines and chemokines.

Indication: For the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy.

There is no pregnancy category for this medication; however, the risk summary indicates that available data from case reports on use in pregnant women are not sufficient to assess for a drug associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. Transport of human IgG antibody across the placenta increases as pregnancy progresses and peaks during the third trimester; thus, Bimzelx® may be transmitted from the mother to the developing fetus. There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to Bimzelx® during pregnancy. For more information, contact the Organization of Teratology Information Specialists (OTIS) AutoImmune Diseases Study at 1-877-311-8972 or visit online. The safety and efficacy of use in the pediatric population have not been established.

Dosage Form: Solution in a single-dose prefilled syringe or single-dose prefilled autoinjector for Injection: 160mg/ml.

Before injecting, remove the carton with Bimzelx® from the refrigerator and allow to reach room temperature (30 to 45 minutes) without removing the prefilled syringes or autoinjectors from the carton (to protect from light). Preservative-free.

Recommended Dosage: Prior to treatment initiation:

- Evaluate patients for tuberculosis (TB) infection.
- Test liver enzymes, alkaline phosphatase, and bilirubin.
- Complete all age-appropriate vaccinations as recommended by current immunization guidelines.

The recommended dosage is 320mg (given as 2 subcutaneous injections of 160mg each) at weeks 0, 4, 8, 12, and 16, then every 8 weeks thereafter. For patients weighing ≥120kg, consider a dosage of 320mg every 4 weeks after week 16. If a dose is missed, administer the dose as soon as possible. Thereafter, resume dosing at the regular scheduled time.

Bimzelx® is intended for use under the guidance and supervision of a healthcare professional. Patients may self-inject after training in subcutaneous injection technique. For each dose, inject two separate 160mg single-dose prefilled syringe or autoinjectors SC at different anatomic locations (such as thighs, abdomen, or back of upper arm). Do not inject within 2 inches of the navel or into areas where the skin is tender, bruised, red, hard, thick, scaly, or affected by psoriasis. Administration in the upper, outer arm may only be performed by a healthcare professional or caregiver.

Drug Interactions: The formation of CYP450 enzymes can be altered by increased levels of certain cytokines (e.g., IL-1, IL-6, IL-10, TNF-alpha) during chronic inflammation. Treatment with Bimzelx® may modulate serum levels of some cytokines. Thus, upon initiation or discontinuation of Bimzelx® in patients who are receiving concomitant drugs which are CYP450 substrates, especially those with a narrow therapeutic index, consider monitoring for effect (e.g., for warfarin) or drug concentration (e.g., for cyclosporine) and consider dosage modification of the CYP450 substrate.

Box Warning: There is no box warning listed with this product.

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions= reported % incidence for drug (Bimzelx®) minus reported % incidence for placebo. Please note that an incidence of 0% means the incidence was the same as or less than placebo.* The most frequently reported adverse events included upper respiratory infection (1%), oral candidiasis (9%), headache (3%), injection site reactions (2%), tinea infections (2%), gastroenteritis (2%), herpes simplex infections (1%), acne (1%), folliculitis (1%), other Candida infections (0%), and fatigue (1%).

Adverse reactions that occurred in <1% but >0.1% of subjects in the Bimzelx® group and at a higher rate than in the placebo group through week 16 were neutropenia, eczema, otitis externa, otitis media, and pyrexia.

During the 16-week, placebo-controlled period of Trials Ps-1 and Ps-2, higher rates of suicidal ideation were reported in Bimzelx®-treated subjects than in placebo-treated subjects. Prescribers should weigh the potential risks and benefits before using Bimzelx® in patients with a history of severe depression or suicidal ideation or behavior. Advise patients, their caregivers, and families to monitor for the emergence or worsening of depression, suicidal ideation, or other mood changes. If such changes occur, advise them to promptly seek medical attention or call the National Suicide and Crisis Lifeline at 988. Bimzelx®-treated patients with new or worsening symptoms of depression or suicidal ideation and/or behavior should be referred to a mental health professional, as appropriate. Prescribers should re-evaluate the risks and benefits of continuing treatment with Bimzelx® if such events occur.

Bimzelx® may increase the risk of infections. Serious infections occurred in 0.3% of subjects treated with Bimzelx® and 0% treated with placebo. Do not start Bimzelx® treatment in patients with any clinically important active infection until the infection resolves or is adequately treated. In patients with a chronic infection or a history of recurrent infection, consider the risks and benefits prior to prescribing Bimzelx®.

Assess patients for tuberculosis (TB) infection prior to starting Bimzelx®. Avoid Bimzelx® use in patients with active TB infection. Start treatment of latent TB prior to administering Bimzelx®. Consider anti-TB treatment prior to starting Bimzelx® in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Closely monitor patients treated with Bimzelx® for signs and symptoms of active TB during and after treatment.

Treatment with Bimzelx® was associated with an increased incidence of liver enzyme elevations as compared with placebo in clinical trials. Elevated liver serum transaminases resolved after Bimzelx® discontinuation. The time to onset of these adverse reactions varied between 28 and 198 days after starting Bimzelx®. Test liver enzymes, alkaline phosphatase, and bilirubin at baseline, periodically during treatment, and per routine patient management. Patients with acute liver disease or cirrhosis may be at increased risk for severe hepatic injury; avoid Bimzelx® use in these patients.

Cases of inflammatory bowel disease (IBD) have been reported in patients treated with IL-17 inhibitors, including Bimzelx®. Avoid Bimzelx® use in patients with active IBD. During Bimzelx® treatment, monitor patients for signs and symptoms of IBD and discontinue treatment if new onset or worsening of signs and symptoms occur.

Prior to starting Bimzelx®, complete all age-appropriate vaccinations per current immunization guidelines. Avoid the use of live vaccines in patients treated with Bimzelx®. Limited data are available regarding the co-administration of Bimzelx® with non-live vaccines.

Contraindications: There are no contraindications listed with this product.

Manufacturer: UCB, Inc.

Analysis: There are 3 multicenter, randomized, double-bind trials (Trial-Ps-1, Trial-Ps-2, and Trial-Ps-3) that assessed the safety and efficacy of Bimzelx® and included adults 18 years of age and older (N=1480) with moderate to severe plaque psoriasis who had a body surface area (BSA) involvement of ≥10%, an Investigator's Global Assessment (IGA) score of ≥3 ('moderate') in the overall assessment of psoriasis on a severity scale of 0 to 4, and a Psoriasis Area and Severity Index (PASI) score ≥12.

In Trial-Ps-1, subjects (N=567) were randomized to receive either Bimzelx® 320mg by SC injection Q4W, ustekinumab (if ≤100kg, 45mg initially and 4 weeks later, then Q12W; if > 100kg, 90mg initially and 4 weeks later, then Q12W), or placebo through week 52. At week 16, subjects originally randomized to placebo received Bimzelx® 320mg Q4W through week 52.

In Trial-Ps-2, subjects (N=435) were randomized to either Bimzelx® 320mg SC Q4W or placebo. At week 16, subjects who achieved a PASI 90 response continued into a 40-week randomized withdrawal period. Subjects originally randomized to Bimzelx® 320mg Q4W were re-randomized to either Bimzelx® 320mg Q4W or Bimzelx® 320mg Q8W or placebo. Subjects originally randomized to placebo continued to receive placebo if they were PASI 90 responders. Subjects who did not achieve a PASI 90 response at week 16 entered an open-label escape arm and received Bimzelx® 320mg Q4W for 12 weeks. Subjects who relapsed, defined as having a less than PASI 75 response compared to baseline, during the randomized withdrawal period also entered the 12-week escape arm.

In Trial-Ps-3, subjects (N=478) were randomized to receive either Bimzelx® 320mg SC injection Q4W through week 56, Bimzelx® 320mg Q4W through week 16 followed by Bimzelx® Q8W through week 56, or adalimumab (80mg as initial dose followed by 40mg QOW starting 1 week after initial dose through week 24) followed by Bimzelx® 320mg Q4W through week 56.

In all 3 trials, 71% of subjects were male, 84% were white, subjects had a mean age of 45 years, and a mean weight of 89kg. At baseline, subjects had a median baseline PASI score of 18, median baseline for BSA of 20%, and baseline IGA score of 4 ("severe') in 33% of subjects. In addition, 93% had psoriasis of the scalp (Scalp IGA score of ≥1), 26% had a history of psoriatic arthritis, and 38% had received prior biologic therapy.

Trial-Ps-1 and Trial-Ps-2 responses at week 16 compared to placebo for the two co-primary endpoints:

- The proportion of subjects who achieved an IGA score 0 ('clear') or 1 ('almost clear') with at least a 2-grade improvement from baseline.
- The proportion of subjects who achieved at least a 90% reduction from baseline PASI (PASI 90).

Secondary endpoints included the proportion of subjects who achieved PASI 100, IGA 0, and Scalp IGA response (defined as Scalp IGA score of 0 [clear] or 1 [almost clear] with at least 2-grade of improvement from baseline) at week 16, and PASI 75 at week 4. In addition, secondary endpoints included assessment of psoriasis symptoms (itching, pain, and scaling) measured by the Patient Symptom Diary (PSD) at week 16.

The proportion of subjects who achieved IGA 0 or 1, PASI 90, IGA 0, and PASI 100 response at week 16 are presented in the table below, which was adapted from the prescribing information.

	Trial-Ps-1		Trial-Ps-2	
Endpoints at week 16	Bimzelx® Q4W (N=321)	Placebo (N=83)	Bimzelx® Q4W (N=349)	Placebo (N=86)
IGA 0 or 1 ('clear' or 'almost clear')	270 (84%)	4 (5%)	323 (93%)	1 (1%)

	Trial-Ps-1		Trial-Ps-2	
Endpoints at week 16	Bimzelx® Q4W (N=321)	Placebo (N=83)	Bimzelx® Q4W (N=349)	Placebo (N=86)
Difference	79%		91%	
NNT *(calculated by CHC)*	2		2	
PASI 90	273 (85%)	4 (5%)	317 (91%)	1 (1%)
Difference	80%		90%	
NNT *(calculated by CHC)*	2		2	
IGA 0 ('clear')	188 (59%)	0 (0%)	243 (70%)	1 (1%)
Difference	59%		69%	
NNT *(calculated by CHC)*	2		2	
PASI 100	188 (59%)	0 (0%)	238 (68%)	1 (1%)
Difference	59%		67%	
NNT *(calculated by CHC)*	2		2	

A greater proportion of subjects randomized to Bimzelx® achieved PASI 75 at week 4 in both trials compared to placebo. In Trial-Ps-1, 77% of subjects treated with Bimzelx® achieved PASI 75 compared to 2% treated with placebo. In Trial-Ps-2, 76% of subjects treated with Bimzelx® achieved PASI 75 compared to 1% treated with placebo.

Among subjects with Scalp IGA score of at least 2 at baseline, a greater proportion of subjects randomized to Bimzelx® achieved Scalp IGA response at week 16 in both trials compared to placebo. In Trial-Ps-1, 84% (240/285) of subjects treated with Bimzelx® achieved Scalp IGA response compared to 15% (11/72) of placebo treated subjects. In Trial-Ps-2, 92% (286/310) of subjects treated with Bimzelx® achieved Scalp IGA response compared to 7% (5/74) of placebo treated subjects.

Maintenance and durability of response were assessed. In Trial-Ps-2, subjects randomized to Bimzelx® Q4W at week 0 and who were PASI 90 responders at week 16 were re-randomized to either continue treatment with Bimzelx® Q4W, switched to Bimzelx® Q8W, or be withdrawn from therapy (i.e., received placebo). The percentage of subjects maintaining IGA 0 or 1 through week 56 after re-randomization at week 16 was 90% with Bimzelx® 320mg Q4W/Bimzelx® 320mg Q8W (N=99), 87% with Bimzelx® 320mg Q4W/Bimzelx® 320mg Q4W (N=105), and 24% with Bimzelx® 320mg Q4W/placebo (N=104).

For IGA 0 or 1 responders at week 16 who were re-randomized to treatment withdrawal (i.e., placebo), the median time to loss of IGA 0 or 1 response was about 24 weeks. Among these subjects with IGA score of 2 at re-treatment, 58% (14/24) achieved IGA score of 0 within 12 weeks of restarting treatment with Bimzelx® 320mg Q4W. Among these subjects with IGA score ≥3 at retreatment, 87% (34/39) regained IGA 0 or 1 response with at least 2-grade improvement from retreatment within 12 weeks of restarting treatment with Bimzelx® 320mg Q4W.

The percentage of subjects maintaining PASI 90 through week 56 after re-randomization at week 16 was 91% with Bimzelx® 320mg Q4W/Bimzelx® 320mg Q8W (N=100), 87% with Bimzelx® 320mg Q4W/Bimzelx® 320mg Q4W (N=106), and 16% with Bimzelx® 320mg Q4W/placebo (N=105).

For PASI 90 responders at week 16 who were re-randomized to treatment withdrawal (i.e., placebo), the median time to loss of PASI 90 response was about 24 weeks.

Greater improvements in itch, pain, and scaling at week 16 with Bimzelx® compared to placebo were observed in both trials as measured by the Patient Symptom Diary (PSD).

Place in Therapy: Bimzelx® is a humanized interleukin-17A and F antagonist indicated for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy. Prior to treatment initiation, assess patients for TB infection; test liver enzymes, alkaline phosphatase, and bilirubin; and complete all age-appropriate vaccinations as recommended by current immunization guidelines.

Three multicenter, randomized, double-blind studies were conducted to assess the safety and efficacy of Bimzelx® in adults with moderate to severe plaque psoriasis who had a BSA involvement of ≥10%, an IGA score of ≥3 in the overall assessment of psoriasis on a severity scale of 0 to 4, and a PASI score ≥12. The co-primary endpoints in Trial-Ps-1 and Trial-Ps-2 included the proportion of subjects who achieved an IGA score of 0 ('clear') or 1 ('almost clear') with at least a 2-grade improvement from baseline, as well as the proportion of subjects who achieved at least a 90% reduction from baseline PASI (PASI 90). Per the full-text by Reich et al[2], a significantly greater proportion receiving bimekizumab than receiving placebo had a PASI 90 and an IGA response at week 16 ($p<0.0001$ for both outcomes). Ustekinumab information was not included in the prescribing information, but per Reich et al[2], a significantly greater proportion receiving bimekizumab than those receiving ustekinumab had a PASI 90 response (85% vs 50%, respectively; $p<0.0001$) and had an IGA response (84% vs 53%, respectively; $p<0.0001$) at week 16.

Information on Trial-Ps-3 was not identified in the Bimzelx® prescribing information. Per the full-text by Warren et al[3], the primary efficacy endpoints were a PASI 90 response at week 16 and an IGA score of 0 or 1 ('clear' or 'almost clear', respectively, with at least a 2-grade improvement from baseline) at week 16. The primary endpoints were assessed for non-inferiority, followed by testing for superiority. Results suggested that for bimekizumab, 86.2% had a PASI 90 response at week 16 as compared with 47.2% receiving adalimumab ($p<0.001$ for non-inferiority and superiority). In addition, 85.3% in the bimekizumab group had an IGA score of 0 or 1 at week 16 (second primary endpoint) as compared with 57.2% in the adalimumab group ($p<0.001$ for non-inferiority and superiority). Bimzelx® was associated with a higher frequency of oral candidiasis and diarrhea as compared with adalimumab, however.

In a randomized, double-blind, active-comparator-controlled study by Reich et al[4], bimekizumab was compared with secukinumab in adults with plaque psoriasis. The primary endpoint was the rate of complete skin clearance, defined as 100% reduction from baseline in the PASI score (PASI 100) at week 16. Bimekizumab was compared for non-inferiority and then superiority. Results suggested that at week 16, 61.7% who received bimekizumab as compared with 48.9% who received secukinumab had a PASI 100 response ($p<0.001$ for non-inferiority and superiority); however, bimekizumab was associated with oral candidiasis.

There is some evidence in a phase 3 study to suggest that Bimzelx® may be more effective than ustekinumab and may be more effective than adalimumab for the endpoints of PASI 90 response and an IGA score of 0 or 1 (with at least a 2-grade improvement from baseline) at week 16. There is also some evidence that Bimzelx® may be more effective than secukinumab in a double-blind study for PASI 100 response; however, there is no evidence at this time to support that Bimzelx® is safer or more effective than all currently preferred, more cost-effective medications. It is therefore recommended that Bimzelx® remain non-preferred and require prior authorization and be available to those who are unable to tolerate or who have failed on preferred medications.

PDL Placement: ☐ **Preferred**
☒ **Non-Preferred with Conditions**

References

[1] Bimzelx® [package insert]. Smyrna, GA: UCB, Inc; 2023.
[2] Reich K, Papp KA, Blauvelt A, et al. Bimekizumab versus ustekinumab for the treatment of moderate to severe plaque psoriasis (BE VIVID): efficacy and safety from a 52-week, multicenter, double-blind, active comparator and placebo-controlled phase 3 trials. *Lancet*. 2021; 397(10273): 487-498.
[3] Warren RB, Blauvelt A, Bagel J, et al. Bimekizumab versus adalimumab in plaque psoriasis. *NEJM*. 2021; 385(2): 130-141.
[4] Reich K, Warren RB, Lebwohl M, et al. Bimekizumab versus secukinumab in plaque psoriasis. NEJM. 2021; 385(2): 142-152.