HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use BIMZELX safely and effectively. See full prescribing information for BIMZELX.

BIMZELX® (bimekizumab-bkzx) injection, for subcutaneous use
Initial U.S. Approval: 2023

----------INDICATIONS AND USAGE----------
BIMZELX is a humanized interleukin-17A and F antagonist indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy. (1)

----------DOSAGE AND ADMINISTRATION----------
- Prior to treatment: (2.1)
  - Evaluate patients for tuberculosis infection.
  - Test liver enzymes, alkaline phosphatase, and bilirubin.
  - Complete all age-appropriate vaccinations as recommended by current immunization guidelines.
- Administer 320 mg (two 160 mg injections) by subcutaneous injection at Weeks 0, 4, 8, 12, and 16, then every 8 weeks thereafter. For patients weighing ≥ 120 kg, consider a dose of 320 mg every 4 weeks after Week 16. (2.2)

----------DOSAGE FORMS AND STRENGTHS----------
Injection: 160 mg/mL in a single-dose prefilled syringe or single-dose prefilled autoinjector. (3)

----------CONTRAINDICATIONS----------
None. (4)

----------WARNINGS AND PRECAUTIONS----------
- Suicidal Ideation and Behavior (SI/B): May increase risk of SI/B. 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. Carefully weigh risks and benefits of treatment with BIMZELX in patients with a history of severe depression and/or suicidal ideation or behavior. (5.1)
- Infections: May increase risk of infection. Instruct patients to seek medical advice if signs or symptoms of clinically important infection occur. If such an infection develops, do not administer BIMZELX until the infection resolves. (5.2)
- Tuberculosis (TB): Avoid use in patients with active TB. Initiate treatment of latent TB prior to BIMZELX treatment. (5.3)
- Liver Biochemical Abnormalities: Elevated serum transaminases were reported in clinical trials. Test liver enzymes, alkaline phosphatase, and bilirubin at baseline and according to routine patient management. Permanently discontinue use of BIMZELX in patients with causally - associated combined elevations of transaminases and bilirubin. (5.4)
- Inflammatory Bowel Disease (IBD): Cases of IBD were reported in clinical trials with IL-17 inhibitors, including BIMZELX. Avoid use of BIMZELX in patients with active IBD. Monitor patients for signs and symptoms of IBD and discontinue treatment if new onset or worsening of signs and symptoms occurs. (5.5)

----------ADVERSE REACTIONS----------
Most common adverse reactions (≥ 1%) are upper respiratory tract infections, oral candidiasis, headache, injection site reactions, tinea infections, gastroenteritis, Herpes simplex infections, acne, folliculitis, other candida infections, and fatigue. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact UCB, Inc. at 844-599-2273 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 10/2023

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the Full Prescribing Information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

BIMZELX is indicated for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Evaluations and Immunization Prior to Treatment Initiation

- Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with BIMZELX *[see Warnings and Precautions (5.3)]*.
- Test liver enzymes, alkaline phosphatase and bilirubin prior to initiating treatment with BIMZELX *[see Warnings and Precautions (5.4)]*.
- Complete all age-appropriate vaccinations as recommended by current immunization guidelines *[see Warning and Precautions (5.6)]*.

2.2 Recommended Dosage

The recommended dosage of BIMZELX is 320 mg (given as 2 subcutaneous injections of 160 mg each) at Weeks 0, 4, 8, 12, and 16, then every 8 weeks thereafter. For patients weighing ≥ 120 kg, consider a dosage of 320 mg every 4 weeks after Week 16 *[see Clinical Pharmacology (12.3)]*.

If a dose is missed, administer the dose as soon as possible. Thereafter, resume dosing at the regular scheduled time.

2.3 Preparation Instructions

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

- Inspect visually for particulate matter and discoloration prior to administration, whenever solution and container permit. BIMZELX injection is clear to slightly opalescent, and colorless to pale brownish- yellow. Do not use if the solution contains visible particles, is discolored or cloudy.

2.4 Administration Instructions

- BIMZELX is intended for use under the guidance and supervision of a healthcare professional. Patients may self-inject after training in subcutaneous injection technique. Provide proper training to patients and/or caregivers on the subcutaneous injection technique of BIMZELX according to the "Instructions for Use" *[see Instructions for Use]*.

- Each prefilled syringe or autoinjector of BIMZELX contains 160 mg of bimekizumab-bkzx. For each dose, inject two separate 160 mg single-dose prefilled syringes or autoinjectors subcutaneously at different anatomic locations (such as thighs, abdomen or back of upper arm). Discard the syringes or autoinjectors after use. Do not reuse.

- Do not inject BIMZELX within 2 inches (5 cm) of the navel or into areas where the skin is tender, bruised, red, hard, thick, scaly, or affected by psoriasis. Administration of BIMZELX in the upper, outer arm may only be performed by a healthcare professional or caregiver.

3 DOSAGE FORMS AND STRENGTHS

Injection: 160 mg/mL clear to slightly opalescent, and colorless to pale brownish-yellow solution in a single-dose prefilled syringe or single-dose prefilled autoinjector.

4 CONTRAINDICATIONS
None.

5 WARNINGS AND PRECAUTIONS
5.1 Suicidal Ideation and Behavior

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.

Suicidal ideation and behavior were prospectively monitored using the Columbia Suicide Severity Rating Scale (C-SSRS) in clinical trials of psoriasis. The C-SSRS is an interview-based instrument used to monitor for the presence and severity of suicidal ideation (ranging from "none" to "active suicidal ideation with specific plan and intent") and behaviors (rating the injury and potential lethality of self-injury, if present). Pooled analysis of C-SSRS data from two 16-week, placebo-controlled clinical trials indicated that 12/670 (1.8%) BIMZELX-treated subjects and 1/169 (0.6%) placebo-treated subjects reported passive suicidal ideation with an estimated relative risk of 3.0 (95% confidence interval: 0.39, 22.74). Subjects without a prior history of SI/B treated with BIMZELX also reported a higher rate of new-onset suicidal ideation on the C-SSRS than subjects treated with placebo (1.3% vs. 0.6%). During the open-label extension trial, one completed suicide was reported in a BIMZELX-treated subject. *[see Adverse Reactions (6.1)]*. A causal association between treatment with BIMZELX and increased risk of suicidal ideation and behavior has not been established.

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 *[see Patient Counseling Information (17)]*. 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 also re-evaluate the risks and benefits of continuing treatment with BIMZELX if such events occur.

5.2 Infections
BIMZELX may increase the risk of infections. In clinical trials in subjects with plaque psoriasis, infections occurred in 36% of the BIMZELX group compared to 23% of the placebo group through 16 weeks of treatment. Upper respiratory tract infections, Candida infections, tinea infections, gastroenteritis, and Herpes Simplex infections occurred more frequently in the BIMZELX group than in the placebo group [*see Adverse Reactions (6.1)*].

Serious infections occurred in 0.3% of subjects treated with BIMZELX and 0% treated with placebo.

Do not initiate treatment with BIMZELX 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. Instruct patients to seek medical advice if signs or symptoms of clinically important infection occur. If a patient develops such an infection or is not responding to standard therapy, monitor the patient closely and discontinue BIMZELX until the infection resolves.

5.3 Tuberculosis
Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with BIMZELX. Avoid the use of BIMZELX in patients with active TB infection. Initiate treatment of latent TB prior to

administering BIMZELX. Consider anti-TB therapy prior to initiation of 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.

5.4 Liver Biochemical Abnormalities
Treatment with BIMZELX was associated with increased incidence of liver enzyme elevations compared to treatment with placebo in randomized clinical trials. Liver serum transaminase elevations > 3 times the upper limit of normal were reported in subjects treated with BIMZELX *[see Adverse Reactions (6.1)]*. Elevated liver serum transaminases resolved after discontinuation of BIMZELX. The time to onset of these adverse reactions varied between 28 and 198 days after starting BIMZELX treatment.

Test liver enzymes, alkaline phosphatase, and bilirubin at baseline, periodically during treatment with BIMZELX and according to routine patient management. If treatment-related increases in liver enzymes occur and drug-induced liver injury is suspected, interrupt BIMZELX until a diagnosis of liver injury is excluded. Permanently discontinue BIMZELX in patients with causally associated combined elevations of transaminases and bilirubin. Patients with acute liver disease or cirrhosis may be at increased risk for severe hepatic injury; avoid use of BIMZELX in these patients.

5.5 Inflammatory Bowel Disease
Cases of inflammatory bowel disease (IBD) have been reported in patients treated with IL-17 inhibitors, including BIMZELX *[see Adverse Reactions (6.1)]*. Avoid use of BIMZELX 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 occurs.

5.6 Immunizations
Prior to initiating therapy with BIMZELX, complete all age-appropriate vaccinations according to current immunization guidelines. Avoid the use of live vaccines in patients treated with BIMZELX. Limited data are available regarding coadministration of BIMZELX with non-live vaccines *[see Clinical Pharmacology (12.2)]*.

6 ADVERSE REACTIONS
The following adverse reactions have been observed with BIMZELX and are discussed in greater detail in other sections of the labeling:

- Suicidal Ideation and Behavior *[see Warnings and Precautions (5.1)]*
- Infections *[see Warnings and Precautions (5.2)]*
- Liver Biochemical Abnormalities *[see Warnings and Precautions (5.4)]*
- Inflammatory Bowel Disease *[see Warnings and Precautions (5.5)]*

6.1 Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

In clinical trials, a total of 1789 subjects with plaque psoriasis were treated with BIMZELX. Of these, 1073 subjects were exposed to BIMZELX for at least one year.

The safety of BIMZELX was evaluated in two placebo-controlled trials (Ps-1 and Ps-2), an active-controlled trial (Ps-3), and an open-label extension trial. Data from Trials Ps-1 and Ps-2 in 839 subjects (mean age 45 years, 72% male, 84% white) were pooled to evaluate the safety of BIMZELX in comparison to placebo up to 16 weeks after treatment initiation. A total of 670 subjects were treated

during this initial period with BIMZELX 320 mg at Weeks 0, 4, 8, 12, and 16. Table 1 summarizes the adverse reactions that occurred at a rate of 1% or greater and at a higher rate in the BIMZELX group than the placebo group.

Table 1: Adverse Reactions Occurring in ≥1% of Subjects with Plaque Psoriasis in the BIMZELX Group and More Frequently than in the Placebo Group in Trials Ps-1 and Ps-2

	BIMZELX N=670 n (%)	**Placebo N=169 n (%)**
URI[a]	102 (15)	24 (14)
Oral Candidiasis[b]	61 (9)	0 (0)
Headache	22 (3)	0 (0)
Injection Site Reactions[c]	19 (3)	2 (1)
Tinea Infections[d]	18 (3)	1 (1)
Gastroenteritis[e]	12 (2)	0 (0)
Herpes Simplex Infections[f]	9 (1)	0 (0)
Acne	8 (1)	0 (0)
Folliculitis	8 (1)	0 (0)
Other Candida Infections[g]	7 (1)	1 (1)
Fatigue	7 (1)	0 (0)

[a] Upper Respiratory Infections include nasopharyngitis, upper respiratory tract infection, pharyngitis, rhinitis, viral upper respiratory tract infection, tonsillitis, sinusitis, pharyngitis streptococcal, pharyngitis bacterial, peritonsillar abscess, viral rhinitis, and influenza

[b] Oral Candidiasis includes oral candidiasis, oropharyngeal candidiasis, oral fungal infection, fungal pharyngitis, and oropharyngitis fungal

[c] Injection Site Reactions include injection site reaction, injection site erythema, injection site pain, injection site edema, injection site bruising, and injection site swelling

[d] Tinea Infections include tinea pedis, fungal skin infection, tinea versicolor, tinea cruris, tinea infection, body tinea, and onychomycosis

[e] Gastroenteritis includes Enterovirus infection, gastroenteritis, gastroenteritis bacterial, and gastroenteritis viral

[f] Herpes Simplex Infections include herpes simplex and oral herpes

[g] Other Candida Infections include vulvovaginal candidiasis, vulvovaginal mycotic infection, skin candida, and genital candidiasis.

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.

The safety of BIMZELX was evaluated in another active-controlled trial (Ps-4) in 743 adult subjects who received BIMZELX 320 mg every 4 weeks or every 8 weeks through Week 48.

Specific Adverse Reactions

Suicidal Ideation and Behavior: The study populations of Trial Ps-1, Trial Ps-2, Trial Ps-3 and Trial Ps-4 excluded subjects with active suicidal ideation, suicidal ideation within the month prior to screening, a history of suicide attempt within the past 5 years prior to screening, or moderately severe to severe major depression (i.e., score of ≥15 on the screening Patient Health Questionnaire-9 (PHQ-9)).

Based on a pooled analysis of the first 16 weeks of the placebo controlled clinical trials, 12 of the 670 subjects in the BIMZELX group (1.8%) reported passive suicidal ideation on the C-SSRS compared to 1 of 169 subjects in the placebo group (0.6%).

During the course of the clinical trials for plaque psoriasis, there was 1 completed suicide in the open label extension trial after 718 days of treatment (1/2480; 0.01/100 subject-years). The completed suicide was reported in a subject without a past reported psychiatric history. There were also 3 suicide attempts (3/2480; 0.04/100 subject-years); 2 of these subjects had a history of prior suicide attempts.

Infections: During the placebo-controlled period of Trials Ps-1 and Ps-2, infections were reported in 36% of subjects (141.7 per 100 patient-years) treated with BIMZELX compared with 23% of subjects (84.6 per 100 patient-years) treated with placebo. Serious infections occurred in 0.3% of subjects (1.0 per 100 patient-years) treated with BIMZELX and 0% treated with placebo.

The most common infections were upper respiratory tract infections and Candida infections, including oral candidiasis (oral candidiasis, oropharyngeal candidiasis, oral fungal infection, fungal pharyngitis, and oropharyngitis fungal) occurring in 9% (30.6 per 100 patient-years) of subjects treated with BIMZELX and other Candida infections (vulvovaginal candidiasis, vulvovaginal mycotic infection, skin candida, and genital candidiasis) in 1% (3.4 per 100 patient-years) of subjects treated with BIMZELX compared to 0% and 1%, respectively, of subjects treated with placebo.

During the combined initial, maintenance, and open-label extension treatment periods of trials Ps-1, Ps-2, Ps-3, and the open-label extension trial, infections were reported in 63% of subjects treated with BIMZELX (120.4 per 100 patient-years). Serious infections were reported in 1.5% of subjects treated with BIMZELX (1.6 per 100 patient-years).

Inflammatory Bowel Disease: In clinical trials in subjects with plaque psoriasis, subjects with active inflammatory bowel disease were excluded. In these trials, which included 2480 subjects exposed to BIMZELX accounting for 5830 patient-years, adjudicated cases of new onset of inflammatory bowel disease (including ulcerative colitis (UC), Crohn's disease (CD) and IBD-undetermined) occurred in seven subjects (0.12 per 100 patient-years); the majority of these cases were serious and resulted in discontinuation of therapy. In clinical development programs for other disease conditions, new cases of Crohn's disease (CD) and UC, some serious, and exacerbations of pre-existing CD and UC, were reported with BIMZELX use.

Liver Biochemical Abnormalities: During the placebo-controlled period of Trials Ps-1 and Ps-2, liver serum transaminase elevations (> 3 times the upper limit of normal [ULN]) occurred in 1.0% of subjects treated with BIMZELX versus 0.6% of subjects treated with placebo. Elevated liver serum transaminases resolved during continued treatment or after discontinuation of BIMZELX.

Safety through Week 56

During the maintenance period (Week 16 through Week 52 of Trial Ps-1 and Week 56 of Trial Ps-2), no new adverse reactions were identified after the initial 16 weeks of treatment. During the maintenance treatment periods of Trial Ps-2 and Trial Ps-3, the rates of adverse reactions were similar between subjects treated with BIMZELX 320 mg every four week and every eight weeks, after the initial 16 weeks of treatment.

Safety through Week 128

During the open-label extension trial, including data from Week 56 through Week 128, new adverse reactions of suicide attempt and a completed suicide occurred.

Additional Safety Data
In an active-controlled clinical trial (Trial Ps-4), 691 subjects with plaque psoriasis were treated with bimekizumab for up to 144 weeks. No new adverse reactions were identified.

7 DRUG INTERACTIONS

CYP450 Substrates
The formation of CYP450 enzymes can be altered by increased levels of certain cytokines (e.g., IL-1, IL-6, IL-10, TNFα, IFN) during chronic inflammation. Treatment with BIMZELX may modulate serum levels of some cytokines.

Therefore, upon initiation or discontinuation of BIMZELX in patients who are receiving concomitant drugs which are CYP450 substrates, particularly 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.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Exposure Registry
There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to BIMZELX during pregnancy. For more information, healthcare providers or patients can contact the Organization of Teratology Information Specialists (OTIS) AutoImmune Diseases Study at 1-877-311-8972 or visit http://mothertobaby.org/pregnancy-studies/.

Risk Summary
Available data from case reports on BIMZELX use in pregnant women are insufficient to evaluate 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; therefore, BIMZELX may be transmitted from the mother to the developing fetus *(see Clinical Considerations)*. In an enhanced pre- and postnatal development study, no adverse developmental effects were observed in infants born to pregnant monkeys after subcutaneous administration of bimekizumab-bkzx during the period of organogenesis through parturition at doses up to 38 times the maximum recommended human dose (MRHD) *(see Data)*.

All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. The background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations
Fetal/Neonatal Adverse Reactions: Because bimekizumab-bkzx may interfere with immune response to infections, risks and benefits should be considered prior to administering live vaccines to infants exposed to BIMZELX in utero. There are no data regarding infant serum levels of bimekizumab-bkzx at birth and the duration of persistence of bimekizumab-bkzx in infant serum after birth. Although a specific timeframe to delay live virus immunizations in infants exposed in utero is unknown, a minimum of 4 months after birth may be considered because of the half-life of the product.

Data
Animal Data: An enhanced pre- and postnatal developmental toxicity study was conducted in cynomolgus monkeys. Pregnant cynomolgus monkeys were administered subcutaneous doses of bimekizumab-bkzx of 20 or 50 mg/kg/week from gestation day 20 to parturition and the cynomolgus monkeys (mother and infants) were monitored for 6 months after delivery. No maternal toxicity was noted in this study. There

were no treatment-related effects on growth and development, malformations, developmental immunotoxicology or neurobehavioral development. The no observed adverse effect level (NOAEL) for both maternal and developmental toxicity was identified as 50 mg/kg/week (38 times the MRHD, based on mg/kg comparison of 1.33 mg/kg/week administered as a 320 mg dose to a 60 kg individual once every 4 weeks).

8.2 Lactation

Risk Summary

There are no data on the presence of bimekizumab-bkzx in human or animal milk, the effects on the breastfed infant, or the effects on milk production. Endogenous IgG and monoclonal antibodies are transferred in human milk. The effects of local gastrointestinal exposure and limited systemic exposure in the breastfed infant to bimekizumab-bkzx are unknown. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for BIMZELX and any potential adverse effects on the breastfed infant from BIMZELX or from the underlying maternal condition.

8.4 Pediatric Use

The safety and effectiveness of BIMZELX in pediatric patients have not been established.

8.5 Geriatric Use

Of the 1789 subjects with plaque psoriasis that were exposed to BIMZELX, a total of 153 subjects were 65 years of age or older, and 18 subjects were 75 years of age or older. Although no differences in safety or effectiveness were observed between subjects 65 years of age or older and younger adult subjects, the number of subjects aged 65 years and over is not sufficient to determine whether they respond differently from younger adult subjects.

11 DESCRIPTION

Bimekizumab-bkzx, an interleukin-17 A and F antagonist, is a recombinant humanized immunoglobulin G1 (IgG1) monoclonal antibody. Bimekizumab-bkzx is produced by recombinant DNA technology in Chinese Hamster Ovary cells, and has an approximate molecular weight of 150 kDa.
BIMZELX (bimekizumab-bkzx) injection is a sterile, preservative-free, clear to slightly opalescent, and colorless to pale brownish-yellow solution for subcutaneous use.

Each BIMZELX prefilled syringe or prefilled autoinjector delivers 1 mL containing 160 mg bimekizumab-bkzx, glacial acetic acid (1.23 mg), glycine (16.5 mg), polysorbate 80 (0.4 mg), sodium acetate (2.83 mg), and Water for Injection, USP at pH 5.1.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Bimekizumab-bkzx is a humanized immunoglobulin IgG1/ κ monoclonal antibody with two identical antigen binding regions that selectively bind to human interleukin 17A (IL-17A), interleukin 17F (IL-17F), and interleukin 17-AF cytokines, and inhibits their interaction with the IL-17receptor 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.

12.2 Pharmacodynamics

Elevated levels of IL-17A and IL-17F are found in lesional psoriatic skin. Bimekizumab-bkzx exposure-response relationships to serum biomarkers, including IL-17A and IL-17F, and the time course of such pharmacodynamic responses are unknown.

Immune Response to Inactivated or Non-Live Vaccines

Healthy individuals who received a single 320 mg dose of BIMZELX two weeks prior to vaccination with an inactivated seasonal influenza vaccine had similar antibody responses compared to individuals who did not receive BIMZELX prior to vaccination. The effectiveness of inactivated seasonal influenza vaccines and other inactivated and non-live vaccines has not been evaluated in patients treated with BIMZELX.

12.3 Pharmacokinetics

The following pharmacokinetic parameters are reported for adult patients with moderate to severe plaque psoriasis, unless otherwise specified. The median peak plasma concentration of bimekizumab-bkzx was 25 (range: 12-50) µg/mL and was reached in 3-4 days. Bimekizumab-bkzx exhibited dose-proportional pharmacokinetics in patients with plaque psoriasis over a dose range of 64 mg to 480 mg (0.2 to 1.5 times the approved recommended dosage) following subcutaneous administration.

Absorption

The absolute bioavailability of bimekizumab-bkzx was 70% in healthy subjects.

Distribution

The median volume of distribution at steady state was 11.2 L.

Elimination

The median (coefficient of variation %) clearance (CL/F) of bimekizumab-bkzx was 0.337 L/day (32.7%). The mean terminal elimination half-life was 23 days, with clearance independent of dose.

Metabolism: Bimekizumab-bkzx is expected to be degraded into small peptides by catabolic pathways.

Specific Populations

No significant differences in the pharmacokinetics of bimekizumab-bkzx were observed based on age (≥18 years).

Body Weight: The average plasma concentration in adult subjects weighing ≥120 kg was predicted to be at least 30% lower than those weighing < 120 kg (median of 87 kg) *[see Dosage and Administration Section (2.2)].*

12.6 Immunogenicity

The observed incidence of anti-drug antibodies (ADA) is highly dependent on the sensitivity and specificity of the assay. Differences in assay methods preclude meaningful comparisons of the incidence of ADA in the studies described below with the incidence of ADA in other studies, including those of BIMZELX or of other bimekizumab products.

During the 52–56-week treatment period in Trial-Ps-1, Trial-Ps-2, and Trial-Ps-3 *[see Clinical Studies (14)],* 116/257 (45%) of BIMZELX-treated subjects (at the recommended dosage) developed anti-bimekizumab-bkzx antibodies (also referred to as ADA). Of the BIMZELX-treated subjects who developed ADA in these trials, approximately 16% had neutralizing antibodies. There was no identified clinically significant effect of ADA on safety or effectiveness of BIMZELX over the treatment duration of 56 weeks.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity and mutagenicity studies have not been conducted with bimekizumab-bkzx.

No effects on fertility parameters such as effects on reproductive organs, menstrual cycle length, or sperm analysis were observed in sexually mature cynomolgus monkeys that were subcutaneously administered

200 mg/kg/week bimekizumab-bkzx (150 times the MRHD, based on mg/kg comparison) for 26 weeks. The monkeys were not mated to evaluate fertility.

14 CLINICAL STUDIES

Three multicenter, randomized, double-blind trials [Trial-Ps-1 (NCT03370133), Trial-Ps-2 (NCT03410992), and Trial-Ps-3 (NCT03412747)] enrolled a total of 1480 subjects 18 years of age and older 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, 567 subjects were randomized to receive either BIMZELX 320 mg by subcutaneous injection every 4 weeks, ustekinumab (for subjects weighing ≤100kg, 45 mg initially and 4 weeks later, then every 12 weeks; for subjects weighing >100kg, 90 mg initially and 4 weeks later, then every 12 weeks), or placebo through Week 52. At Week 16, subjects originally randomized to placebo received BIMZELX 320 mg every 4 weeks through Week 52.

In Trial-Ps-2, 435 subjects were randomized to either BIMZELX 320 mg by subcutaneous injection every 4 weeks 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 320 mg every 4 weeks were re-randomized to either BIMZELX 320 mg every 4 weeks or BIMZELX 320 mg every 8 weeks 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 320 mg every 4 weeks 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, 478 subjects were randomized to receive either BIMZELX 320 mg by subcutaneous injection every 4 weeks through week 56, BIMZELX 320 mg every 4 weeks through week 16 followed by BIMZELX every 8 weeks through week 56, or adalimumab (80 mg as an initial dose followed by 40 mg every other week starting 1 week after initial dose through Week 24) followed by BIMZELX 320 mg every 4 weeks through Week 56.

In Trial-Ps1, Trial-Ps-2, and Trial-Ps-3, 71% of the subjects were male and 84% of the subjects were White, with a mean age of 45 years and a mean weight of 89 kg. 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. A total of 93% subjects had psoriasis of the scalp (Scalp IGA score of ≥1) and a total of 26% of subjects had a history of psoriatic arthritis. Additionally, 38% had received prior biologic therapy.

Clinical Response at Week 16 (Trial-Ps-1 and Trial-Ps-2)

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 of 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 Table 2.

Table 2: Efficacy Results at Week 16 in BIMZELX- or Placebo-Treated Adults with Plaque Psoriasis in Trial-Ps-1 and Trial-Ps-2

	Trial-Ps-1		Trial-Ps-2	
	BIMZELX 320 mg every 4 weeks (N=321) n (%)	**Placebo (N=83) n (%)**	**BIMZELX 320 mg every 4 weeks (N=349) n (%)**	**Placebo (N=86) n (%)**
IGA 0 or 1 ("clear" or "almost clear") [a]	270 (84%)	4 (5%)	323 (93%)	1 (1%)
Difference (95% CI)	79% (73%, 85%)		91% (88%, 95%)	
PASI 90[a]	273 (85%)	4 (5%)	317 (91%)	1 (1%)
Difference (95% CI)	80% (74%, 86%)		90% (86%, 93%)	
IGA 0 ("clear")	188 (59%)	0 (0%)	243 (70%)	1 (1%)
Difference (95% CI)	59% (53%, 64%)		69% (64%, 74%)	
PASI 100	188 (59%)	0 (0%)	238 (68%)	1 (1%)
Difference (95% CI)	59% (53%, 64%)		67% (62%, 73%)	

[a] Co-primary endpoints

Examination of age, gender, race, baseline IGA score and previous treatment with systemic or biologic agents did not identify differences in response to BIMZELX among these subgroups at Week 16.

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.

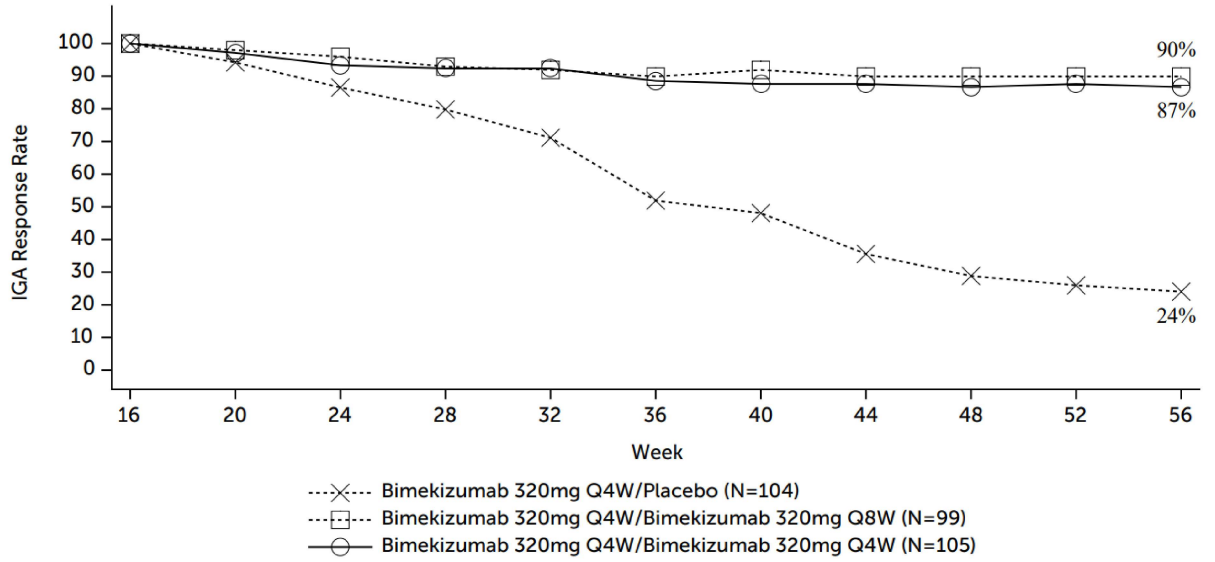
Among subjects with Scalp IGA score of at least 2 at baseline, a greater proportion of subjects randomized to BIMZELX achieved Scalp IGA response at Week 16 in both trials compared to placebo. In Trial-Ps-1, 84% (240/285) of subjects treated with BIMZELX achieved Scalp IGA response compared to 15% (11/72) 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

In Trial-Ps-2, subjects randomized to BIMZELX every 4 weeks at Week 0 and who were PASI 90 responders at Week 16 were re-randomized to either continue treatment with BIMZELX every 4 weeks, switched to BIMZELX every 8 weeks, or be withdrawn from therapy (i.e., received placebo).

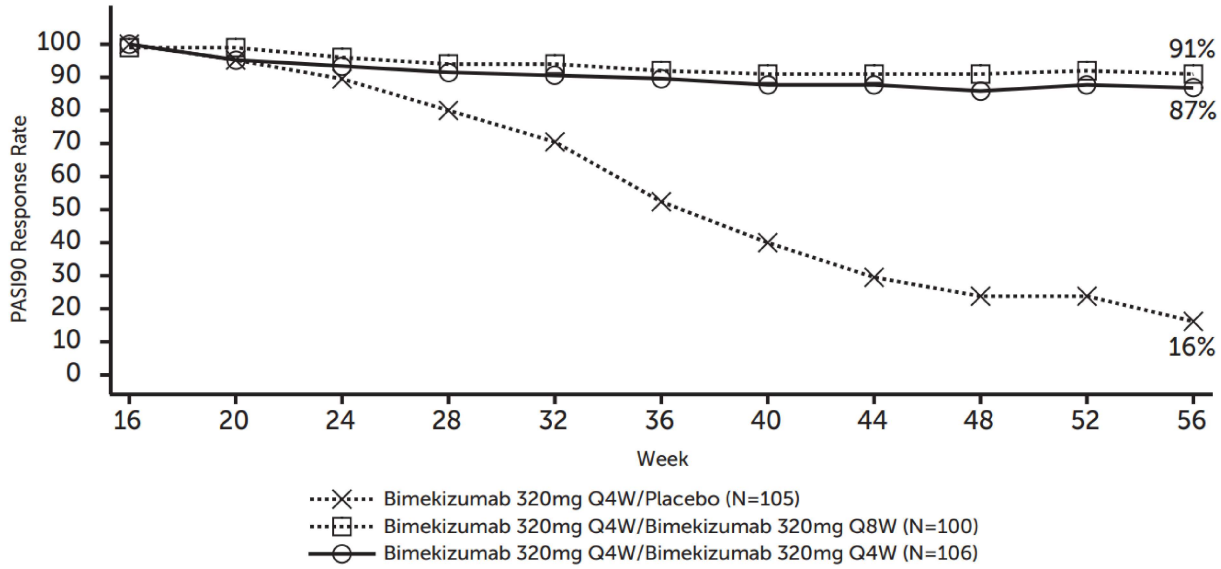
Figure 1 and Figure 2 present the percentage of subjects maintaining IGA score of 0 ("Clear") or 1 ("Almost Clear") and PASI 90, respectively, through Week 56 after re-randomization at Week 16.

Figure 1: Percentage of Subjects Maintaining IGA 0 or 1 through Week 56 after Re-Randomization at Week 16



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 approximately 24 weeks. Among these subjects with IGA score of 2 at retreatment, 58% (14/24) achieved IGA score of 0 within 12 weeks of restarting treatment with BIMZELX 320 mg every 4 weeks. 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 320 mg every 4 weeks.

Figure 2: Percentage of Subjects Maintaining PASI 90 through Week 56 after Re-Randomization at Week 16



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 approximately 24 weeks.

Patient Reported Outcomes

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).

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

BIMZELX (bimekizumab-bkzx) injection is a sterile, preservative-free, clear to slightly opalescent, and colorless to pale brownish-yellow solution. Each prefilled autoinjector or prefilled syringe contains 1 mL of a 160mg/mL solution. BIMZELX is supplied as:

BIMZELX autoinjector:

- NDC 50474-781-85: Carton of two 160 mg/mL single-dose autoinjectors. Each prefilled autoinjector is fixed with a 27 gauge ½ inch needle.

BIMZELX prefilled syringe:

- NDC 50474-780-79: Carton of two 160 mg/mL single-dose prefilled syringes. Each prefilled syringe is fixed with a 27 gauge ½ inch needle with needle guard.

Storage and Handling

Store cartons with BIMZELX refrigerated between 2°C to 8°C (36°F to 46°F). Keep the product in the original carton to protect it from light until the time of use. Do not freeze. Do not shake. Do not use beyond expiration date. BIMZELX does not contain a preservative; discard any unused portion. Not made with natural rubber latex.

When necessary, BIMZELX prefilled syringes or autoinjectors may be stored at room temperature up to 25°C (77°F) in the original carton for a single period of up to 30 days. Once BIMZELX prefilled syringes or autoinjectors have been stored at room temperature, do not place back in refrigerator. Write the date removed from the refrigerator in the space provided on the carton and discard if not used within a 30-day period.

17 PATIENT COUNSELING INFORMATION

Advise the patient and/or caregiver to read the FDA-approved patient labeling (Medication Guide and Instructions for Use).

Administration Instructions

Instruct patients or caregivers to perform the first self-injection under the supervision and guidance of a qualified healthcare professional for proper training in subcutaneous injection technique *[see Dosage and Administration (2.4), Instructions for Use]*.

Instruct patients or caregivers to administer two 160 mg single-dose syringes or two 160 mg single-dose autoinjectors to achieve the 320 mg dose of BIMZELX *[see Dosage and Administration (2.4)]*.

Instruct patients or caregivers in the technique of needle and syringe disposal *[see Instructions for Use]*.

Advise patients if they forget to take their dose of BIMZELX to inject their dose as soon as they remember. Instruct patients to then take their next dose at the appropriate scheduled time *[see Dosage and Administration (2.2)]*.

Suicidal Ideation and Behavior

Instruct patients and their caregivers to monitor for the emergence of suicidal ideation and behavior and promptly seek medical attention if the patient experiences suicidal ideation or behavior; or new onset or worsening depression, anxiety, or other mood changes. Instruct patients to call the National Suicide and Crisis Lifeline at 988 if they experience suicidal ideation or behavior. *[see Warnings and Precautions (5.1)]*.

Infections
Inform patients that BIMZELX may lower the ability of their immune system to fight infections. Instruct patients of the importance of communicating any history of infections to the healthcare provider and contacting their healthcare provider if they develop any symptoms of an infection *[see Warnings and Precautions (5.2)]*.

Liver Biochemical Abnormalities
Inform patients that BIMZELX may increase the risk of elevated liver enzymes. Acute liver disease or cirrhosis may increase this risk. Advise patients that laboratory evaluation is needed prior to and periodically during treatment. Advise patients to hold the next dose of BIMZELX and call their healthcare provider right away, if signs or symptoms of liver dysfunction occur. *[see Warnings and Precautions (5.4)]*.

Inflammatory Bowel Disease
Instruct patients to seek medical advice if they develop signs and symptoms of Crohn's disease or ulcerative colitis *[see Warnings and Precautions (5.5)]*.

Immunizations
Advise patients that vaccination with live vaccines is not recommended during BIMZELX treatment. Instruct patients to inform their healthcare practitioner that they are taking BIMZELX prior to a potential vaccination *[see Warnings and Precautions (5.6)]*.

Pregnancy
Advise patients that there is a pregnancy registry that monitors pregnancy outcomes in women exposed to BIMZELX during pregnancy *[see Use in Specific Populations (8.1)]*.

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