CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761151Orig1s000

PRODUCT QUALITY REVIEW(S)

BLA Executive Summary
Assessment Date: May 19, 2023

1. Application/Product Information

BLA number	761151
Submission Type	Resubmission
Regulatory Pathway	NME 351(a)
Associated IND/BLA	IND128707
Review Designation	Standard Review
Applicant	UCB, Inc.
Indication	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.
Rx/OTC dispensed	Rx
Drug Product Name	Proprietary Name: BIMZELX
	Non-proprietary Name: BIMZELX
	OBP Naming: MAB HUMAN (IGG1) ANTI Q16552 (IL17_HUMAN) & ANTI Q96PD4 (IL17F_HUMAN) [UCB4940]
Drug Product Description	BIMZELX (BIMZELX) injection is a sterile, preservative-free, clear to slightly opalescent and pale brownish-yellow solution for subcutaneous use. Each BIMZELX pre-filled safety syringe or pre-filled autoinjector delivers 1 mL containing 160 mg BIMZELX, (b) (4) (1.23 mg), glycine (16.5 mg), polysorbate 80 (0.40 mg), sodium acetate (b) (4) and Water for Injection, USP at pH (b) (4) Liquid drug product contained within a glass pre-filled syringe (PFS) is further packaged into one of two commercial presentations, a safety syringe (SS) or an autoinjector (AI).
Dosage Form	Liquid
Strength	160 mg/mL
Route of Administration	Subcutaneous Injection
Primary Container Closure System	Pre-filled Syringe
Device Information	(1) single-dose safety syringe and (2) single-dose autoinjector
Co-packaged Product Information	N/A

	Discipline	Primary	Secondary
OPQ Review Team	Drug substance	Xuhong Li	Kelley Burridge
	Drug product		
	Immunogenicity Assay		
	Facility	Wayne Seifert	Zhong Li
	Microbiology	DS: Bo Chi DP: Wayne Seifert	Maxwell Van Tassell
	RBPM	Erica Keafer	
	ATL	Kelley Burridge	
OPQ Issued Consults	CDRH: Porsche Bennett		

2. Recommendation and Conclusion on Approvability
Recommendation: Approval

The Office of Pharmaceutical Quality, CDER, recommends approval of BLA 761151 for BIMZELX manufactured by UCB, Inc. The data submitted in this application are adequate to support the conclusion that the manufacture of BIMZELX is well-controlled and leads to a product that is pure and potent. It is recommended that this product be approved for human use under conditions specified in the package insert.

3. CMC Information for Action Letter

a. Manufacturing Location:

- **Drug Substance:** [redacted] (b) (4)
- **Drug Product:**
  - Manufacturer: UCB Pharma SA, Chemin du Foriest, Braine-l'Alleud, Belgium; FEI:14203003909356
  - Secondary packaging, labeling, and storage: [redacted] (b) (4)

b. Fill size and dosage form: BIMZELX is supplied as 160 mg/mL solution in a safety syringe and autoinjector.

c. Dating Period:

- **Drug Product:** 36 months at 2 to 8°C with storage up to 30 days at 25°C permitted within the expiry
- **Drug Substance:** [redacted] (b) (4) months at [redacted] (b) (4)
- **For packaged products:** Not co-packaged

d. Exempt from lot release:

- Yes

- Rationale: BIMZELX is exempted from lot release per FR 95-29960.

4. Basis for Recommendation

Summary: BIMZELX is designed to treat moderate to severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy. BIMZELX was statistically superior to placebo (p-values < 0.001) for both co-primary efficacy endpoints in both clinical trials. The Applicant demonstrated that BIMZELX is effective for its intended use in the target population.

BIMZELX, an interleukin-17 A and F antagonist, is an immunoglobulin G1 (IgG1) monoclonal antibody produced by recombinant DNA technology in Chinese Hamster Ovary cells. BIMZELX is a humanized IgG1/κ monoclonal antibody that selectively binds to human interleukin 17A (IL-17A), interleukin 17F (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 involved in normal inflammatory and immune responses. BIMZELX inhibits the release of proinflammatory cytokines and chemokines.

(b) (4)

(b) (4)

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(b) (4)

(b) (4)

The manufacturing processes and overall control strategies for BIMZELX are appropriately established to ensure consistency and quality of the final product; therefore, lot variability is not a concern. The assays used for immunogenicity assessment in the clinical studies to support this BLA are adequately validated and suitable for their intended purpose. The BLA is recommended for approval from the product quality, facility, microbiology and sterility assurance perspectives.

a. Subdiscipline Recommendation:

Drug Substance	**-**	**Adequate**
Drug Product	**-**	**Adequate**
Immunogenicity Assay	**-**	**Adequate**
Facilities	**-**	**Adequate**
Microbiology	**-**	**Adequate**

b. Environmental Assessment (EA):
Categorical exclusion is claimed by the applicant and deemed acceptable.

c. Potency Assessment for Labeling:
As an initial matter, we determined that no U.S. standard of potency has been prescribed for BIMZELX (i.e., there is no specific test method described in regulation for BIMZELX that establishes an official standard of potency). We next considered whether potency is a factor for BIMZELX within the meaning of 21 CFR 610.61(r), which requires a statement about potency on the package (carton) label if "potency is a factor" and "no U.S. standard of potency has been prescribed." We have determined that potency is not a factor for BIMZELX for purposes of § 610.61(r) because lot variability is not a concern for BIMZELX as BIMZELX's manufacturing process is appropriately controlled to ensure the consistency and quality of the final product.

5. Life-Cycle Considerations

a. Established Conditions based on ICH Q12 principles: No

b. Drug Substance:

i. Protocols approved:

1. (b) (4)
2.
3. Annual Stability Protocol

ii. Residual risk: None

iii. Future inspection points to consider: None

c. Drug Product:

i. Protocols approved: See protocols for DS noted above.

ii. Residual risk: None

(b) (4)

FOIA statement: More detailed assessments of the BLA submission, which are not included in this integrated quality assessment, may be requested via a Freedom of Information Act (FOIA) request.

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

KELLEY A BURRIDGE
05/19/2023 04:17:13 PM

Recommendation: Complete Response

BLA Number: 761151
Assessment Number: 1
Assessment Date: May 6, 2022

Drug Name/Dosage Form	BIMZELX (bimekizumab-bkzx) injection, for subcutaneous use in (1) single-dose prefilled syringe and (2) single-dose autoinjector
Strength/Potency	160 mg/mL
Route of Administration	Subcutaneous injection
Rx/OTC dispensed	Rx
Indication	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.
Recommended Dosing Regimen	320 mg (two 160 mg injections) administered by subcutaneous injection at Weeks 0, 4, 8, 12 and 16, then every 8 weeks thereafter. For patients weighing ≥120 kg, a dose of 320 mg every 4 weeks after week 16 may be considered.
Applicant/Sponsor	UCB, Inc.
US agent, if applicable	N/A

Product Overview:

Bimekizumab-bkzx, an interleukin-17 A and F antagonist, is an immunoglobulin G1 (IgG1) monoclonal antibody produced by recombinant DNA technology in Chinese Hamster Ovary cells. Bimekizumab-bkzx is a humanized IgG1/κ monoclonal antibody that selectively binds to human interleukin 17A (IL-17A), interleukin 17F (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 involved in normal inflammatory and immune responses. Bimekizumab-bkzx inhibits the release of proinflammatory cytokines and chemokines.

BIMZELX (bimekizumab-bkzx) injection is a sterile, preservative-free, clear to slightly opalescent and pale brownish-yellow solution for subcutaneous use. Each BIMZELX prefilled syringe or prefilled autoinjector delivers 1 mL containing 160 mg bimekizumab-bkzx, (b) (4) (1.23 mg), glycine (16.5 mg), polysorbate 80 (0.40 mg), sodium acetate (b) (4) and Water for Injection, USP at pH (b) (4). Liquid drug product contained within a glass pre-filled syringe (PFS) is further packaged into one of two commercial presentations, a safety syringe (SS) or an autoinjector (AI).

Quality Assessment Team:

Discipline	Primary Assessor	Secondary Assessor	Branch/Division
Drug Substance	Xuhong Li	Kelley Burridge	CDER/OPQ/OBP/DBRRIV
Drug Product			
Immunogenicity			
Labeling	James Barlow Jennifer Kim		CDER/OPQ/OBP
Facility	Wayne Seifert	Zhong Li	CDER/OPQ/OPMA/DBM
Microbiology-Drug Substance	Bo Chi	Candace Gomez-Broughton	
Microbiology-Drug Product	Wayne Seifert		
Devices (Consult)	Matthew Ondeck	Rumi Young	CDRH/OPEQ/OHTIII/DHTIIIC
Application Team Lead	Kelley Burridge		CDER/OPQ/OBP/DBRRIV
RBPM	Erica Keafer, Anh-Thy Ly		CDER/OPQ/OPRO/DRBPMI/RBPMB1

Multidisciplinary Assessment Team:

Discipline	Assessor	Team Leader	Office/Division
RPM	Strother Dixon		CDER/OND/ORO/DROII
Cross-disciplinary Team Lead	Gordana Diglisic		CDER/OND/OII/DDD
Medical Officer	Kevin Clark	Gordana Diglisic	CDER/OND/OII/DDD
Pharmacology/Toxicology	Jill Merrill	Barbara Hill	CDER/OND/OII/DPTII
Clinical Pharmacology	Jie (Jenny) Cheng	Chinmay Shukla	CDER/OTS/OCP/DIIP
Statistics	Marilena Flouri	Mohamed Alosh	CDER/OTS/OB/DBIII

1. Names:

   a. Proprietary Name: BIMZELX
   b. Trade Name: BIMZELX
   c. Non-Proprietary Name/USAN: bimekizumab-bkzx
   d. CAS Name: 1418205-77-2
   e. Common Name: UCB4940 (CDP4940)
   f. INN Name: bimekizumab-bkzx
   g. OBP systematic name: MAB HUMAN (IGG1) ANTI Q16552 (IL17_HUMAN) & ANTI Q96PD4 (IL17F_HUMAN) [UCB4940]

Submissions Assessed:

Submission(s) Assessed	Document Date
STN 761151/0001 - New/BLA	July 15, 2020
STN 761151/0002 - Labeling/Package Insert Draft	July 16, 2020
STN 761151/0004 - Quality/Response To Information Request	July 29, 2020
STN 761151/0005 - Quality/Response To Information Request	August 12, 2020
STN 761151/0006 - Quality/Response To Information Request	August 19, 2020
STN 761151/0009 - Quality/Response To Information Request	September 24, 2020
STN 761151/0011 - General Correspondence	September 29, 2020
STN 761151/0012 - Quality/Response To Information Request	October 2, 2020
STN 761151/0013 - Quality/Quality Information	October 8, 2020
STN 761151/0015 - Quality/Response To Information Request	October 15, 2020
STN 761151/0018 - Quality/Response To Information Request	November 12, 2020
STN 761151/0019 - General Correspondence	November 20, 2020
STN 761151/0020 - Quality/Response To Information Request	November 25, 2020
STN 761151/0021 - Quality/Response To Information Request	December 3, 2020
STN 761151/0026 - Quality/Response To Information Request	January 11, 2021
STN 761151/0032 - Quality/Quality Information	January 26, 2021
STN 761151/0037 - Quality/Response To Information Request	February 12, 2021
STN 761151/0041 - Quality/Response To Information Request	March 1, 2021
STN 761151/0043 - Quality/Response To Information Request	March 11, 2021
STN 761151/0044 - Quality/Response To Information Request	March 16, 2021
STN 761151/0049 - Quality/Quality Information	April 19, 2021
STN 761151/0050 - Quality/Quality Information	May 3, 2021
STN 761151/0051 - Labeling/Container-Carton Draft, Labeling/Package Insert Draft	May 19, 2021

STN 761151/0052 - Quality/Response To Information Request	June 28, 2021
STN 761151/0054 - Labeling/Container-Carton Draft	August 13, 2021
STN 761151/0055 - Quality/Quality Information	August 23, 2021
STN 761151/0056 - Labeling/Container-Carton Draft	September 7, 2021
STN 761151/0057 - Quality/Response to Information Request	September 30, 2021
STN 761151/0056 - Labeling/Container-Carton Draft	November 30, 2021
STN 761151/0056 - Labeling/Container-Carton Draft	January 25, 2022
STN 761151/0056 - Labeling/Container-Carton Draft	January 31, 2022
STN 761151/0056 - Labeling/Package Insert Draft	March 2, 2022

Quality Assessment Data Sheet:

1. Legal Basis for Submission: 351(a)
2. Related/Supporting Documents:

   A. DMFs:

DMF #	DMF Type	DMF Holder	Item referenced	Code[1]	Status[2]	Date Assessment Completed	Comments
(b) (4)	II	(b) (4)		3	N/A	N/A	LOA June 1, 2020
	II			3	N/A	N/A	LOA May 29, 2020
	II			3	N/A	N/A	LOA May 22, 2020
	II			3	N/A	N/A	LOA June 1, 2020
	III			3	N/A	N/A	LOA August 14, 2019
	III			3	N/A	N/A	LOA August 16, 2019

		(b) (4)				
(b) (4)	III		3	N/A	N/A	LOA November 8, 2019

1. Action codes for DMF Table: 1- DMF Assessed; Other codes indicate why the DMF was not assessed, as follows: 2- Assessed previously and no revision since last assessment; 3- Sufficient information in application; 4- Authority to reference not granted; 5- DMF not available; 6- Other (explain under "comments")

2. Action codes for Status column: Adequate, Adequate with Information Request, Deficient, or N/A (There is not enough data in the application; therefore, the DMF did not need to be assessed.

B. Other documents: IND, Referenced Listed Drug (RLD), or sister application.

Document	Application Number	Description
IND	128707	Investigation of the use of UCB4940 for the treatment of patients with psoriasis. Initially submitted on June 14, 2016.
(b) (4)		

3. Consults:

Discipline/Topic	Date Requested	Status	Recommendation	Assessor
CDRH/Devices Safety syringe and autoinjector	July 20, 2020	Complete	Approvable pending device inspection at UCB Pharma SA	Matthew Ondeck (primary) Rumi Young (secondary)

4. Environmental Assessment of Claim of Categorical Exclusion: Acceptable per 21 CFR 25.31(c)

Executive Summary:

I. Recommendations:

A. Recommendation and Conclusion on Approvability:

This application will not be approved during this assessment cycle due to GMP deficiencies identified during inspection of the UCB Braine Drug Product Manufacturing Facility (FEI: 3003909356) by the Office of Pharmaceutical Manufacturing Assessment/Division of Biotechnology Manufacturing (OPMA/DBM). At this time, there are no outstanding module 3 review issues from either OBP or OPMA for STN 761151 for BIMZELX (bimekizumab-bkzx) manufactured by UCB, Inc. Because the application will not be approved in this cycle, the facility issue listed below will be communicated to the sponsor in the FDA Complete Response (CR) letter. If manufacturing changes are made before the sponsor submits their responses to the CR deficiencies, additional assessment may be needed during the next assessment cycle.

B. Summary of Complete Response Issues:

OPMA/DBM has completed the compliance reviews of the pre-license inspections conducted at [redacted] (b) (4) & UCB Braine Drug Product Manufacturing Facility (FEI: 3003909356). The inspectional recommendation will be a withhold for the UCB Braine Drug Product site as a result of the inadequate 483 responses. The [redacted] (b) (4) site 483 responses were deemed adequate and the site is acceptable. The Overall Manufacturing Inspection Recommendation (OMIR) for this BLA will be "Withhold" due to the withhold approval recommendation for the UCB Braine Drug Product manufacturing site.

C. CR Action Letter Language:

We have completed our review of this application, as amended, and have determined that we cannot approve this application in its present form. We have described our reasons for this action below and, where possible, our recommendations to address these issues.

FACILITY INSPECTIONS

During a recent inspection of the UCB Pharma SA (FEI: 3003909356) manufacturing facility for this application, our field investigator conveyed deficiencies to the representative of the facility. Satisfactory resolution of these deficiencies is required before this application may be approved.

D. Benefit/Risk Considerations:

Bimekizumab-bkzx drug product is a monoclonal antibody designed to treat moderate to severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy. Bimekizumab-bkzx was statistically superior to placebo (p-values < 0.001) for both co-primary efficacy endpoints in both clinical trials. The Applicant demonstrated that bimekizumab-bkzx is effective for its intended use in the target population.

E. Recommendation on Phase 4 (Post-Marketing) Commitments, Requirements, Agreements, and/or Risk Management Steps, if approvable: None.

II. Summary of Quality Assessments:

A. CQA Identification, Risk and Lifecycle Knowledge Management

Table 1: Active Pharmaceutical Ingredient CQA Identification, Risk and Lifecycle Knowledge Management

Type of CQA	Quality Attribute	Risk	Origin	Control Strategy
Identity*	Identity	Safety	Intrinsic to molecule	(b) (4)
Appearance	Degree of Clarity and Opalescence	DP Stability	Formulation	
	Degree of Coloration			
Strength	Protein Concentration	Biological Activity, Safety	Formulation	
Potency	IL-17A Activity IL-17F Activity	Stability, biological activity, PK/PD	Intrinsic to molecule, in-process and on DP stability	
Product Variants - Size	Low Molecular Weight Species	Biological Activity, PK/PD, stability	Protein isoforms. Potentially impacted by in-process conditions, formulation, and on stability.	
	High Molecular Weight Species and Proteinaceous Sub-visible Particulates	Biological activity, PK/PD, immunogenicity, safety, stability		
Product Variants - Charge	Deamidated Variants in CDR	Biological activity, PK/PD, stability	Protein isoforms.	
	Deamidated Variants in FcRn Contact Region	PK/PD, stability	(b) (4)	

Type of CQA	Quality Attribute	Risk	Origin	Control Strategy
			(b) (4)	(b) (4)
	Glycation and Advanced Glycation End Products in CDR	Biological activity, PK/PD	Protein isoforms (b) (4) .	
	Glycation and Advanced Glycation End Products in FcRn Contact Region	PK/PD		
Product Variants - Glycosylation	Non-glycosylated Variants	PK/PD	Protein isoforms. Post-translational modifications during (b) (4) No change in glycan profile expected on stability. (b) (4) .	
	High (b) (4) Variants		Protein isoforms. Post-translational modifications during (b) (4) No change in glycan profile expected on stability. (b) (4) Impacted by the (b) (4)	
Product Variants - Oxidation	Oxidation of (b) (4)	PK/PD	Protein isoforms. (b) (4)	

Type of CQA	Quality Attribute	Risk	Origin	(b) (4)
	Oxidation of [redacted] (b) (4)	Biological activity, PK/PD	Protein isoforms.	
Product Variants - Other	Misincorporation of Amino Acids	Biological activity, PK/PD, immunogenicity, safety	Protein isoforms.	
	[redacted] (b) (4)			
Physicochemical Properties	pH	Stability	Formulation. Potentially impacted by in-process conditions and on DP stability.	
Process-related Impurities	[redacted] (b) (4)	Safety, purity	Process, raw materials, container closure system	
Microbiological Contaminants	Bacterial Endotoxins	Safety, purity	Process, raw materials	

Type of CQA	Quality Attribute	Risk	Origin	Control Strategy
				(b) (4)
	Bioburden	Safety, purity Efficacy due to degradation or modification of the product by microbial contamination.		
(b) (4)				
Contaminants	Cross Contamination With Other Active Products	Safety	Manufacture in multi-product facilities	

*Not a CQA but testing required by regulatory expectations.

B. Drug Substance [bimekizumab-bkzx] Quality Summary

Table 2: Drug Substance CQA Process Risk Identification and Lifecycle Knowledge Management

Type of CQA	Quality Attribute	Risk	Origin	Control Strategy
Process-related Impurities	Host Cell Protein (HCP)	Stability, immunogenicity, safety	(b) (4)	(b) (4)

Type of CQA	Quality Attribute	Risk	Origin	Control Strategy
				(b) (4)
	Host Cell DNA	Immunogenicity, safety		
	(b) (4)	Immunogenicity, safety, PK/PD	(b) (4)	
	(b) (4)	Safety	(b) (4)	
Contaminants	(b) (4)	Safety	Production bioreactor, potentially from environment.	
	(b) (4)			
	Transmissible (b) (4)	Safety	Raw materials of animal origin	

- Description: Bimekizumab-bkzx is a genetically engineered, humanized, full length IgG1 antibody with high affinity for human IL-17A and IL-17F. The antibody contains two light chains and two heavy chains with a nominal theoretical molecular mass of 149,886 Da. Each light chain contains 214 amino acids while each heavy chain contains 455 amino acids. Bimekizumab-bkzx contains 32 cysteines which form 16 total disulfide bonds, four inter-chain and twelve intra-chain. The predominant species, considered the desired product, is as follows: clipped C-terminal lysine residue on the heavy chain, no pyroglutamic acid at the N-terminus of the heavy chain, and Fc region with core fucosylated, agalactosylated/ monogalactosylated, bi-antennary complex type glycan (G0F/G1F). Glycosylation is N-linked to Asn 305 on the heavy chain. In vitro and in vivo data collected in toxicology and clinical studies support the absence of in vivo effector functions for bimekizumab-bkzx.

- Mechanism of Action (MoA): Bimekizumab-bkzx is a humanized IgG1/κ monoclonal antibody that selectively binds to human interleukin 17A (IL-17A), interleukin 17F (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 involved in normal inflammatory and immune responses. Bimekizumab-bkzx inhibits the release of proinflammatory cytokines and chemokines.

- Relative Potency Assays: To fulfill its biological function, the antibody needs to bind and neutralize both IL-17A and IL-17F. Cell-based assays using a reporter gene quantitatively measure the relative potency of bimekizumab-bkzx in a human embryonic kidney (HEK)-Blue™ IL-17 cell line exposed to either recombinant human IL-17A or IL-17F. HEK-Blue IL-17 cells generated by stably introducing human genes for the IL-17 receptor express IL-17RA/IL-17RC heterodimer. HEK-Blue IL-17 cells also express a secreted embryonic alkaline phosphatase (SEAP) reporter gene placed under the control of the IFN-β minimal promoter fused to five NF-κB and five AP-1 binding sites. Binding of IL-17 to IL-17RA/IL-17RC on the surface of HEK-Blue IL-17 cells triggers a signaling cascade leading to activation of NF-κB and AP-1 which, in turn, induces the reporter gene (SEAP). SEAP is quantified using QUANTI-Blue™ with a colorimetric readout proportional to the bimekizumab-bkzx concentration. Results are reported as percentage binding activity (% relative potency) relative to the reference standard. Master and working cell banks are in place for the HEK-Blue IL-17 cells used in the assays.

- Reference Materials: A one-tier, primary in-house RS is currently in place for commercial use and is acceptable for the following reasons: (b) (4)

- Critical starting materials or intermediates: (b) (4)

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- Manufacturing process summary: (b) (4)

(b) (4)

- Container closure: (b) (4)
- Dating period and storage conditions: (b) (4) months at (b) (4)

C. Drug Product [BIMZELX] Quality Summary:

Table 3: Drug Product CQA Identification, Risk, and Lifecycle Management

Type of CQA	Quality Attribute	Risk	Origin	Control Strategy (b) (4)
Particles	Visible Particles	Stability	Formulation. Potentially from process or environment.	
	Subvisible Particles (b) (4)	Stability, safety	Formulation, protein precipitation	
Physicochemical Properties	Osmolality	Safety	Formulation	
	Extractable Volume	Dosing accuracy	Filling process, container closure system properties	
Syringe Functionality	Break-loose Force	Human factors/usability	Container closure system properties	
	Gliding Force			
Safety Syringe Feature	Safety Feature Activation Force*	Human factors/usability, safety	Syringe safety device properties	

Type of CQA	Quality Attribute	Risk	Origin	Control Strategy
Autoinjector	Injection Time* Actuation Force* Needle Extension*	Human factors/usability	Autoinjector device properties	(b) (4) [redacted]
Microbiological Contaminants and Sterility Assurance	Sterility	Safety, purity Efficacy due to degradation or modification of the product by microbial contamination.	Process, failure of container closure integrity, breach during manufacture or storage.	

*Not a CQA.

- Potency and Strength: 160 mg/mL solution of bimekizumab-bkzx in a single-use prefilled safety syringe or single-use autoinjector
- Summary of Product Design: Sterile, preservative-free, clear to slightly opalescent, pale brownish-yellow solution injected subcutaneously to deliver 160 mg of bimekizumab-bkzx.
- List of Excipients: (b) (4) [redacted] (1.23 mg), glycine (16.5 mg), polysorbate 80 (0.40 mg), sodium acetate (b) (4) [redacted] and Water for Injection, USP
- Reference Materials: (b) (4) [redacted]
- Manufacturing process summary: (b) (4) [redacted]

(b) (4) [redacted]

(b) (4)

- Container closure: Liquid drug product is contained within a clear, 1 mL, type (b) (4) borosilicate glass pre-filled syringe fitted with a staked, 27G, ½" thin wall needle closed with a grey, (b) (4) rubber stopper and a rigid needle shield consisting of a (b) (4) elastomer needle cover and a (b) (4) rigid shield. The two presentations are (1) a safety syringe and (2) an autoinjector. The safety syringe consists of the pre-filled syringe plus a plunger rod, small round flange sub-assembly, extended finger flange, and overcap sub-assembly. The autoinjector consists of a pre-filled syringe plus a cap remover sleeve, housing cover, syringe unit, and drive unit.

- Dating period and storage conditions: 36 months at 2 to 8°C with storage up to 30 days at 25°C permitted within the expiry

- List of co-package components, if applicable: N/A

D. Novel Approaches/Precedents: None

E. Any Special Product Quality Labeling Recommendations:

- Store cartons with BIMZELX refrigerated between 2° to 8°C (36° 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 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 77° F (25° C) 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.

F. Establishment Information:

Overall Recommendation: Withhold					
Function	Site Information	FEI Number	Preliminary Assessment	Inspectional Observations	Final Recommendation
Storage of master and WCB; manufacture and storage of DP, final assembly of finished product; secondary packaging and labeling; quality control testing of DS (back-up), DP, and finished product; stability testing of DS	UCB Pharma SA Chemin du Foriest Braine-l'Alleud, Belgium 1420	3003909356	PLI	See UCB Pharma SA Inspection Observations	Withhold - Based on PLI

(back-up testing of samples only), DP, and finished product; batch release of DS, DP, and finished product.					
Master and WCB production and storage, DS manufacture, quality control testing of DS and DP (back-up), and stability testing of DS and DP (back-up testing of samples only).	(b) (4)		PLI	See (b) (4)	Approve - Based on PLI
In-process testing: (b) (4)			Approve - Based on Previous History	Approve - Based on Previous History	Approve - Based on Previous History
Secondary packaging, labeling, and storage of finished product.			Approve - Based on Previous History District File Review	Approve - Based on Previous History District File Review	Approve - Based on Previous History District File Review

UCB Pharma SA Inspection Observations: 1) Failure to establish process controls designed to assure that the drug product you manufacture has the identity, strength, quality, and purity that it purports or is represented to possess; 2) Control procedures are not established which monitor the output of those manufacturing processes that may be responsible for causing variability in the characteristic of in-process material and the drug product; 3) A utility is of inadequate design; and 4) A facility is not adequately maintained.

(b) (4)

G. Facilities:

Following the OPMA/DBM review of the application and inspectional documents, there are significant, outstanding manufacturing risks that prevent approval of this application. Satisfactory resolution of the cited deficiencies for the proposed drug product manufacturing

facility, UCB Pharma SA, Braine-l'Alleud, Belgium (FEI: 3003909356), during a recent FDA inspection, is required before this application may be approved.

Adequate descriptions of the facility, equipment, environmental controls, cleaning and contamination control strategy were provided for (b) (4) .
All proposed testing facilities are acceptable based on their current acceptable CGMP compliance.

H. Lifecycle Knowledge Management:

a. Drug Substance:

i. Protocols approved:

Post-approval Change Management Protocols (PACMPs)
1. (b) (4)
2.

ii. Outstanding assessment issues/residual risk: See inspection point below from the DS review.

iii. Future inspection point to consider:

1. (b) (4)

b. Drug Product

i. Protocols approved: See protocols for DS noted above.

ii. Outstanding assessment issues/residual risk: See inspection point below from the DP review.

iii. Future inspection point to consider:

1. (b) (4)

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/s/

KELLEY A BURRIDGE
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Recommendation: Approval Pending Inspections

BLA Number: 761151
Assessment Number: 1
Assessment Date: October 14, 2021

Drug Name/Dosage Form	BIMZELX (bimekizumab-bkzx) injection, for subcutaneous use in (1) single-dose prefilled syringe and (2) single-dose autoinjector
Strength/Potency	160 mg/mL
Route of Administration	Subcutaneous injection
Rx/OTC dispensed	Rx
Indication	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.
Recommended Dosing Regimen	320 mg (two 160 mg injections) administered by subcutaneous injection at Weeks 0, 4, 8, 12 and 16, then every 8 weeks thereafter. For patients weighing ≥120 kg, a dose of 320 mg every 4 weeks after week 16 may be considered.
Applicant/Sponsor	UCB, Inc.
US agent, if applicable	N/A

Product Overview:

Bimekizumab-bkzx, an interleukin-17 A and F antagonist, is an immunoglobulin G1 (IgG1) monoclonal antibody produced by recombinant DNA technology in Chinese Hamster Ovary cells. Bimekizumab-bkzx is a humanized IgG1/κ monoclonal antibody that selectively binds to human interleukin 17A (IL-17A), interleukin 17F (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 involved in normal inflammatory and immune responses. Bimekizumab-bkzx inhibits the release of proinflammatory cytokines and chemokines.

BIMZELX (bimekizumab-bkzx) injection is a sterile, preservative-free, clear to slightly opalescent and pale brownish-yellow solution for subcutaneous use. Each BIMZELX prefilled syringe or prefilled autoinjector delivers 1 mL containing 160 mg bimekizumab-bkzx, (b) (4) (1.23 mg), glycine (16.5 mg), polysorbate 80 (0.40 mg), sodium acetate (b) (4) and Water for Injection, USP at pH (b) (4) Liquid drug product contained within a glass pre-filled syringe (PFS) is further packaged into one of two commercial presentations, a safety syringe (SS) or an autoinjector (AI).

Quality Assessment Team:

Discipline	Primary Assessor	Secondary Assessor	Branch/Division
Drug Substance	Xuhong Li	Kelley Burridge	CDER/OPQ/OBP/DBRRIV
Drug Product			
Immunogenicity			
Labeling	James Barlow		CDER/OPQ/OBP
Facility	Wayne Seifert	Zhong Li	CDER/OPQ/OPMA/DBM
Microbiology-Drug Substance	Bo Chi	Candace Gomez-Broughton	
Microbiology-Drug Product	Wayne Seifert		
Devices (Consult)	Matthew Ondeck	Rumi Young	CDRH/OPEQ/OHTIII/DHTIIIC
Application Team Lead	Kelley Burridge		CDER/OPQ/OBP/DBRRIV
RBPM	Erica Keafer, Anh-Thy Ly		CDER/OPQ/OPRO/DRBPMI/RBPMB1

Multidisciplinary Assessment Team:

Discipline	Assessor	Team Leader	Office/Division
RPM	Strother Dixon		CDER/OND/ORO/DROII
Cross-disciplinary Team Lead	Gordana Diglisic		CDER/OND/OII/DDD
Medical Officer	Kevin Clark	Gordana Diglisic	CDER/OND/OII/DDD
Pharmacology/Toxicology	Jill Merrill	Barbara Hill	CDER/OND/OII/DPTII
Clinical Pharmacology	Jie (Jenny) Cheng	Chinmay Shukla	CDER/OTS/OCP/DIIP
Statistics	Marilena Flouri	Mohamed Alosh	CDER/OTS/OB/DBIII

1. Names:

   a. Proprietary Name: BIMZELX
   b. Trade Name: BIMZELX
   c. Non-Proprietary Name/USAN: bimekizumab-bkzx
   d. CAS Name: 1418205-77-2
   e. Common Name: UCB4940 (CDP4940)
   f. INN Name: bimekizumab-bkzx
   g. OBP systematic name: MAB HUMAN (IGG1) ANTI Q16552 (IL17_HUMAN) & ANTI Q96PD4 (IL17F_HUMAN) [UCB4940]

Submissions Assessed:

Submission(s) Assessed	Document Date
STN 761151/0001 - New/BLA	July 15, 2020
STN 761151/0002 - Labeling/Package Insert Draft	July 16, 2020
STN 761151/0004 - Quality/Response To Information Request	July 29, 2020
STN 761151/0005 - Quality/Response To Information Request	August 12, 2020
STN 761151/0006 - Quality/Response To Information Request	August 19, 2020
STN 761151/0009 - Quality/Response To Information Request	September 24, 2020
STN 761151/0011 - General Correspondence	September 29, 2020
STN 761151/0012 - Quality/Response To Information Request	October 2, 2020
STN 761151/0013 - Quality/Quality Information	October 8, 2020
STN 761151/0015 - Quality/Response To Information Request	October 15, 2020
STN 761151/0018 - Quality/Response To Information Request	November 12, 2020
STN 761151/0019 - General Correspondence	November 20, 2020
STN 761151/0020 - Quality/Response To Information Request	November 25, 2020
STN 761151/0021 - Quality/Response To Information Request	December 3, 2020
STN 761151/0026 - Quality/Response To Information Request	January 11, 2021
STN 761151/0032 - Quality/Quality Information	January 26, 2021
STN 761151/0037 - Quality/Response To Information Request	February 12, 2021
STN 761151/0041 - Quality/Response To Information Request	March 1, 2021
STN 761151/0043 - Quality/Response To Information Request	March 11, 2021
STN 761151/0044 - Quality/Response To Information Request	March 16, 2021
STN 761151/0049 - Quality/Quality Information	April 19, 2021
STN 761151/0050 - Quality/Quality Information	May 3, 2021
STN 761151/0051 - Labeling/Container-Carton Draft, Labeling/Package Insert Draft	May 19, 2021
STN 761151/0052 - Quality/Response To Information Request	June 28, 2021

STN 761151/0054 - Labeling/Container-Carton Draft	August 13, 2021
STN 761151/0055 - Quality/Quality Information	August 23, 2021
STN 761151/0056 - Labeling/Container-Carton Draft	September 7, 2021
STN 761151/0057 - Quality/Response to Information Request	September 30, 2021

Quality Assessment Data Sheet:

1. Legal Basis for Submission: 351(a)
2. Related/Supporting Documents:

   A. DMFs:

DMF #	DMF Type	DMF Holder	Item referenced	Code[1]	Status[2]	Date Assessment Completed	Comments
(b) (4)	II	(b) (4)		3	N/A	N/A	LOA June 1, 2020
	II			3	N/A	N/A	LOA May 29, 2020
	II			3	N/A	N/A	LOA May 22, 2020
	II			3	N/A	N/A	LOA June 1, 2020
	III			3	N/A	N/A	LOA August 14, 2019
	III			3	N/A	N/A	LOA August 16, 2019

			bromobutyl rubber stopper				
(b) (4)	III	(b) (4)		3	N/A	N/A	LOA November 8, 2019

1. Action codes for DMF Table: 1- DMF Assessed; Other codes indicate why the DMF was not assessed, as follows: 2- Assessed previously and no revision since last assessment; 3- Sufficient information in application; 4- Authority to reference not granted; 5- DMF not available; 6- Other (explain under "comments")

2. Action codes for Status column: Adequate, Adequate with Information Request, Deficient, or N/A (There is not enough data in the application; therefore, the DMF did not need to be assessed.

B. Other documents: IND, Referenced Listed Drug (RLD), or sister application.

Document	Application Number	Description
IND	128707	Investigation of the use of UCB4940 for the treatment of patients with psoriasis. Initially submitted on June 14, 2016.
(b) (4)		

3. Consults:

Discipline/Topic	Date Requested	Status	Recommendation	Assessor
CDRH/Devices Safety syringe and autoinjector	July 20, 2020	Complete	Approvable pending device inspection at UCB Pharma SA	Matthew Ondeck (primary) Rumi Young (secondary)

4. Environmental Assessment of Claim of Categorical Exclusion: Acceptable per 21 CFR 25.31(c)

Executive Summary:

I. Recommendations:

A. Recommendation and Conclusion on Approvability:

Pending the outcome of pre-license inspections, the Office of Pharmaceutical Quality (OPQ), CDER, recommends approval of STN 761151 for BIMZELX (bimekizumab-bkzx) manufactured by UCB, Inc. The data submitted in this application are adequate pending inspections to support the conclusion that the manufacture of BIMZELX is well-controlled and leads to a product that is pure and potent. It is recommended that this product be approved for human use under conditions specified in the package insert pending successful outcomes of inspections.

Summary of Complete Response Issues: None.

Approval Action Letter Language: No action at this time. Pending inspections.

Benefit/Risk Considerations:
Bimekizumab-bkzx drug product is a monoclonal antibody designed to treat moderate to severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy. Bimekizumab-bkzx was statistically superior to placebo (p-values < 0.001) for both co-primary efficacy endpoints in both clinical trials. The Applicant demonstrated that bimekizumab-bkzx is effective for its intended use in the target population.

Due to the COVID-19 pandemic, we were unable to perform pre-license inspections on the DS manufacturing site (b) (4) and the DP manufacturing site UCB in Belgium. This BLA cannot be approved until inspections are completed.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Requirements, Agreements, and/or Risk Management Steps, if approvable: None, pending inspections.

II. Summary of Quality Assessments:

A. CQA Identification, Risk and Lifecycle Knowledge Management

Table 1: Active Pharmaceutical Ingredient CQA Identification, Risk and Lifecycle Knowledge Management

Type of CQA	Quality Attribute	Risk	Origin	Control Strategy (b) (4)
Identity*	Identity	Safety	Intrinsic to molecule	
Appearance	Degree of Clarity and Opalescence	DP Stability	Formulation	
	Degree of Coloration			

Type of CQA	Quality Attribute	Risk	Origin	Control Strategy (b) (4)
Strength	Protein Concentration	Biological Activity, Safety	Formulation	
Potency	IL-17A Activity IL-17F Activity	Stability, biological activity, PK/PD	Intrinsic to molecule, in-process and on DP stability	
Product Variants - Size	Low Molecular Weight Species	Biological Activity, PK/PD, stability	Protein isoforms. Potentially impacted by in-process conditions, formulation, and on stability.	
	High Molecular Weight Species and (b) (4) Sub-visible Particulates	Biological activity, PK/PD, immunogenicity, safety, stability		
Product Variants - Charge	Deamidated Variants in CDR	Biological activity, PK/PD, stability	Protein isoforms. (b) (4)	
	Deamidated Variants in FcRn Contact Region	PK/PD, stability		
	Glycation and Advanced Glycation End Products in CDR	Biological activity, PK/PD	(b) (4) .	
	Glycation and Advanced Glycation End Products in FcRn Contact Region	PK/PD		
Product Variants - Glycosylation	Non-glycosylated Variants	PK/PD	Protein isoforms. Post-translational modifications during (b) (4) No change in glycan profile expected on stability.	

Type of CQA	Quality Attribute	Risk	Origin	Control Strategy
			Impacted by (b) (4)	(b) (4)
	(b) (4) Variants		Protein isoforms. Post-translational modifications during (b) (4) . No change in glycan profile expected on stability. (b) (4) . Impacted by the (b) (4)	
Product Variants - Oxidation	Oxidation of (b) (4)	PK/PD	Protein isoforms. (b) (4) .	
	Oxidation of (b) (4)	Biological activity, PK/PD	Protein isoforms.	
Product Variants - Other	Misincorporation of Amino Acids	Biological activity, PK/PD, immunogenicity, safety	Protein isoforms.	

Type of CQA	Quality Attribute	Risk	Origin	Control Strategy
				(b) (4)
	(b) (4)			
Physicochemical Properties	pH	Stability	Formulation. Potentially impacted by in-process conditions and on DP stability.	
Process-related Impurities	(b) (4)	Safety, purity	Process, raw materials, container closure system	
Microbiological Contaminants	Bacterial Endotoxins	Safety, purity	Process, raw materials	
	Bioburden	Safety, purity Efficacy due to degradation or modification of the product by microbial contamination.		
			(b) (4)	

Type of CQA	Quality Attribute	Risk	Origin	Control Strategy
	[redacted] (b) (4)			[redacted] (b) (4)
Contaminants	Cross Contamination With Other Active Products	Safety	Manufacture in multi-product facilities	

*Not a CQA but testing required by regulatory expectations.

B. Drug Substance [bimekizumab-bkzx] Quality Summary

Table 2: Drug Substance CQA Process Risk Identification and Lifecycle Knowledge Management

Type of CQA	Quality Attribute	Risk	Origin	Control Strategy
Process-related Impurities	Host Cell Protein (HCP)	Stability, immunogenicity, safety	[redacted] (b) (4)	[redacted] (b) (4)
	Host Cell DNA	Immunogenicity, safety		
	[redacted] (b) (4)	Immunogenicity, safety, PK/PD	[redacted] (b) (4)	
	[redacted] (b) (4)	Safety	[redacted] (b) (4)	

Type of CQA	Quality Attribute	Risk	Origin	Control Strategy
				(b) (4)
Contaminants	(b) (4)	Safety	(b) (4)	
	(b) (4)			
	(b) (4)	Safety	(b) (4)	

- Description: Bimekizumab-bkzx is a genetically engineered, humanized, full length IgG1 antibody with high affinity for human IL-17A and IL-17F. The antibody contains two light chains and two heavy chains with a nominal theoretical molecular mass of 149,886 Da. Each light chain contains 214 amino acids while each heavy chain contains 455 amino acids. Bimekizumab-bkzx contains 32 cysteines which form 16 total disulfide bonds, four inter-chain and twelve intra-chain. The predominant species, considered the desired product, is as follows: clipped C-terminal lysine residue on the heavy chain, no pyroglutamic acid at the N-terminus of the heavy chain, and Fc region with core fucosylated, agalactosylated/ monogalactosylated, bi-antennary complex type glycan (G0F/G1F). Glycosylation is N-linked to Asn 305 on the heavy chain. In vitro and in vivo data collected in toxicology and clinical studies support the absence of in vivo effector functions for bimekizumab-bkzx.

- Mechanism of Action (MoA): Bimekizumab-bkzx is a humanized IgG1/κ monoclonal antibody that selectively binds to human interleukin 17A (IL-17A), interleukin 17F (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 involved in normal inflammatory and immune responses. Bimekizumab-bkzx inhibits the release of proinflammatory cytokines and chemokines.

- Relative Potency Assays: To fulfill its biological function, the antibody needs to bind and neutralize both IL-17A and IL-17F. Cell-based assays using a reporter gene quantitatively measure the relative potency of bimekizumab-bkzx in a human embryonic kidney (HEK)-Blue™ IL-17 cell line exposed to either recombinant human IL-17A or IL-17F. HEK-Blue IL-17 cells generated by stably introducing human genes for the IL-17 receptor express IL-17RA/IL-17RC heterodimer. HEK-Blue IL-17 cells also express a secreted embryonic alkaline phosphatase (SEAP) reporter gene placed under the control of the IFN-β minimal promoter fused to five NF-κB and five AP-1 binding sites. Binding of IL-17 to IL-17RA/IL-17RC on the surface of HEK-Blue IL-17 cells triggers a signaling cascade leading to activation of NF-κB and AP-1 which, in turn, induces the reporter gene (SEAP). SEAP is quantified using QUANTI-Blue™ with a colorimetric readout proportional to the bimekizumab-bkzx concentration. Results are reported as percentage binding activity (% relative potency) relative to the reference standard. Master and working cell banks are in place for the HEK-Blue IL-17 cells used in the assays.

- Reference Materials: A one-tier, primary in-house RS is currently in place for commercial use and is acceptable for the following reasons: (b) (4)

- Critical starting materials or intermediates: (b) (4)

- Manufacturing process summary: (b) (4)

- Container closure: [redacted] (b) (4)
- Dating period and storage conditions: [redacted] (b) (4) months at [redacted] (b) (4)

C. Drug Product [BIMZELX] Quality Summary:

Table 3: Drug Product CQA Identification, Risk, and Lifecycle Management

Type of CQA	Quality Attribute	Risk	Origin	Control Strategy
Particles	Visible Particles	Stability	Formulation. Potentially from process or environment.	[redacted] (b) (4)
	Subvisible Particles [redacted] (b) (4)	Stability, safety	Formulation, protein precipitation	
Physicochemical Properties	Osmolality	Safety	Formulation	
	Extractable Volume	Dosing accuracy	Filling process, container closure system properties	
Syringe Functionality	Break-loose Force	Human factors/usability	Container closure system properties	
	Gliding Force			
Safety Syringe Feature	Safety Feature Activation Force*	Human factors/usability, safety	Syringe safety device properties	
Autoinjector	Injection Time*	Human factors/usability	Autoinjector device properties	
	Actuation Force*			
	Needle Extension*			

Type of CQA	Quality Attribute	Risk	Origin	Control Strategy
Microbiological Contaminants and Sterility Assurance	Sterility	Safety, purity Efficacy due to degradation or modification of the product by microbial contamination.	Process, failure of container closure integrity, breach during manufacture or storage.	(b) (4) [redacted]

*Not a CQA.

- Potency and Strength: 160 mg/mL solution of bimekizumab-bkzx in a single-use prefilled safety syringe or single-use autoinjector
- Summary of Product Design: Sterile, preservative-free, clear to slightly opalescent, pale brownish-yellow solution injected subcutaneously to deliver 160 mg of bimekizumab-bkzx.
- List of Excipients: (b) (4) [redacted] (1.23 mg), glycine (16.5 mg), polysorbate 80 (0.40 mg), sodium acetate (b) (4) [redacted] and Water for Injection, USP
- Reference Materials: (b) (4) [redacted].
- Manufacturing process summary: (b) (4) [redacted]

(b) (4)

- Container closure: Liquid drug product is contained within a clear, 1 mL, type (b) (4) borosilicate glass pre-filled syringe fitted with a staked, 27G, ½" thin wall needle closed with a grey, (b) (4) rubber stopper and a rigid needle shield consisting of a (b) (4) elastomer needle cover and a (b) (4) rigid shield. The two presentations are (1) a safety syringe and (2) an autoinjector. The safety syringe consists of the pre-filled syringe plus a plunger rod, small round flange sub-assembly, extended finger flange, and overcap sub-assembly. The autoinjector consists of a pre-filled syringe plus a cap remover sleeve, housing cover, syringe unit, and drive unit.

- Dating period and storage conditions: 36 months at 2 to 8°C with storage up to 30 days at 25°C permitted within the expiry

- List of co-package components, if applicable: N/A

D. Novel Approaches/Precedents:

Due to the COVID-19 pandemic, we were unable to perform pre-license inspections on the DS manufacturing site Rentschler in Germany or the DP manufacturing site UCB in Belgium.

E. Any Special Product Quality Labeling Recommendations:

- Store cartons with BIMZELX refrigerated between 2° to 8°C (36° 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 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 77° F (25° C) 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.

F. Establishment Information:

Overall Recommendation: Pending Inspections					
Function	Site Information	FEI Number	Preliminary Assessment	Inspectional Observations	Final Recommendation
Storage of master and WCB; manufacture and storage of DP, final assembly of finished product; secondary packaging and labeling; quality control testing of DS (back-up), DP, and finished product; stability testing of DS	UCB Pharma SA Chemin du Foriest Braine-l'Alleud, Belgium 1420	3003909356	PLI	TBD	Pending PLI

(back-up testing of samples only), DP, and finished product; batch release of DS, DP, and finished product.					
Master and WCB production and storage, DS manufacture, quality control testing of DS and DP (back-up), and stability testing of DS and DP (back-up testing of samples only).	(b) (4)		PLI	TBD	Pending PLI
In-process testing: (b) (4)			Approve - Based on Previous History	Approve - Based on Previous History	Approve - Based on Previous History
Secondary packaging, labeling, and storage of finished product.			Approve - Based on Previous History District File Review	Approve - Based on Previous History District File Review	Approve - Based on Previous History District File Review

G. Facilities:

The facility assessment recommendation is pending, (b) (4) UCB Pharma S.A. FEI: 3003909356 that includes a device inspection, respectively, to be completed upon lifting of COVID-19 travel restrictions.

H. Lifecycle Knowledge Management:

a. Drug Substance:

i. Protocols approved:

Post-approval Change Management Protocols (PACMPs)
1. (b) (4)
2.

ii. Outstanding assessment issues/residual risk: See inspection points below plus the DS and DS microbiology reviews for items needing follow up during the pre-license inspection.

iii. Future inspection points to consider: Pre-license inspection not yet conducted.

(b) (4)

(b) (4)

b. Drug Product

i. Protocols approved: See protocols for DS noted above.

ii. Outstanding assessment issues/residual risk: See inspection points below plus the DP and DP microbiology reviews for items needing follow up during the pre-license inspection.

iii. Future inspection points to consider: Pre-license inspection not yet conducted.

(b) (4)

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/s/

KELLEY A BURRIDGE
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