CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761373Orig2s000
761425Orig2s000

OTHER REVIEW(S)

LABEL AND LABELING REVIEW

Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

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Date of This Review:	April 23, 2025
Requesting Office or Division:	Office of Therapeutic Biologics and Biosimilars (OTBB)
Application Type and Number:	BLA 761373/Ori-2, BLA 761425/Ori-2, BLA 761373/S-004
Product Name, Dosage Form, and Strength:	Pyzchiva (ustekinumab-ttwe) injection, Prefilled syringe: 45 mg/0.5 mL and 90 mg/mL Vial: 45 mg/0.5 mL and 130 mg/26 mL (5 mg/mL)
Product Type:	Combination Product (Biologic-Device)
Rx or OTC:	Prescription (Rx)
Applicant Name:	Samsung Bioepis Co., Ltd.
FDA Received Date:	October 31, 2024 and January 7, 2025
TTT ID #:	2025-13028
DMEPA 1 Safety Evaluator:	Madhuri R. Patel, PharmD
DMEPA 1 Team Leader:	Yevgeniya Kogan, PharmD, BCSCP

1 INTRODUCTION

As part of the approval process for Pyzchiva (ustekinumab-ttwe) injection BLA 761373/Original 2 and BLA 761425/Original 2 for interchangeability designation of Pyzchiva prefilled syringes (45 mg/0.5 mL and 90 mg/mL) and 130 mg/26 mL vial, and Chemistry Manufacturing and Controls (CMC) – Prior Approval Supplement (PAS) BLA 761373/S-004 for interchangeability designation of the Pyzchiva 45 mg/0.5 mL vial, the Office of Therapeutic Biologics and Biosimilars (OTBB) requested that we review the proposed Pyzchiva Prescribing Information (PI), Medication Guide (MG), Instructions for Use (IFU), container labels, and carton labeling for areas of vulnerability that may lead to medication errors. Of note, the acceptability of the labels and labeling from a medication error perspective for (b) (4) and BLA 761425/S-004 (interchangeability designation of Pyzchiva autoinjector 45 mg/0.5 mL and 90 mg/mL) will be evaluated under a separate cover.

1.1 BACKGROUND

Pyzchiva (ustekinumab-ttwe) is a proposed 351(k)(4) interchangeable and the US-licensed Reference Product (RP) is Stelara (ustekinumab), BLA 125261 and BLA 761044.

2 CONCLUSION

We find the Pyzchiva Prescribing Information (PI), Medication Guide (MG), Instructions for Use (IFU) acceptable and the container labels, and carton labeling remain unchanged from what DMEPA previously found acceptable under BLA 761373/Ori-1, BLA 761425/Ori-1, and BLA 761373/S-002.[a,b,c,d] We have no recommendations at this time.

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[a] Patel, M. Review of Revised Label and Labeling for Pyzchiva (BLA 761373 and BLA 761425). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2024 APR 30. TTT ID No.: 2023-4843-1 and 2024-8044.

[b] Patel, M. Review of Revised Label and Labeling for Pyzchiva (BLA 761373 and BLA 761425). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2024 JUN 10. TTT ID No.: 2023-4843-3 and 2024-8044-2.

[c] Patel, M. Label and Labeling Review for Pyzchiva (BLA 761373/S-002 and BLA 761425/S-002). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2024 NOV 07. TTT ID No.: 2024-10689.

[d] Patel, M. Review of Revised Label and Labeling for Pyzchiva (BLA 761373/S-002 and BLA 761425/S-002). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2024 DEC 16. TTT ID No.: 2024-10689-2.

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/s/

MADHURI R PATEL
04/23/2025 08:24:42 AM

YEVGENIYA M KOGAN
04/23/2025 11:23:01 AM

MEMORANDUM
REVIEW OF REVISED LABEL AND LABELING

Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

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Date of This Review:	June 10, 2024
Requesting Office or Division:	Division of Dermatology and Dentistry (DDD)
Application Type and Number:	BLA 761373 and BLA 761425
Product Name, Dosage Form, and Strength:	Pyzchiva (ustekinumab-ttwe) injection, 45 mg/0.5 mL and 90 mg/mL prefilled syringe and 130 mg/26 mL (5 mg/mL) vial
Applicant Name:	Samsung Bioepis Co., Ltd
FDA Received Date:	June 7, 2024
TTT ID #:	2023-4843-3 and 2024-8044-2
DMEPA 1 Safety Evaluator:	Madhuri R. Patel, PharmD
DMEPA 1 Team Leader:	Yevgeniya Kogan, PharmD, BCSCP

1 PURPOSE OF MEMORANDUM

Samsung Bioepis Co., Ltd submitted revised container labels and carton labeling received on June 7, 2024 for Pyzchiva. The Division of Dermatology and Dentistry (DDD) requested that we review the revised container labels and carton labeling for Pyzchiva (Appendix A) to determine if they are acceptable from a medication error perspective. The revisions are in response to recommendations that we made during a previous label and labeling review.[a]

2 CONCLUSION

Samsung Bioepis Co., Ltd implemented all of our recommendations and we have no additional recommendations at this time.

4 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

[a] Patel, M. Label and Labeling Review for Pyzchiva (BLA 761373 and BLA 761425). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2024 JUN 03. TTT ID: 2023-4843-3 and 2024-8044-2.

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MADHURI R PATEL
06/10/2024 03:43:17 PM

YEVGENIYA M KOGAN
06/11/2024 07:34:00 AM

MEMORANDUM
REVIEW OF REVISED LABEL AND LABELING

Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

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Date of This Review:	June 3, 2024
Requesting Office or Division:	Division of Dermatology and Dentistry (DDD)
Application Type and Number:	BLA 761373 and BLA 761425
Product Name, Dosage Form, and Strength:	Pyzchiva (ustekinumab-ttwe)[a] injection, 45 mg/0.5 mL and 90 mg/mL prefilled syringe and 130 mg/26 mL (5 mg/mL) vial
Applicant Name:	Samsung Bioepis Co., LTD
FDA Received Date:	May 22, 2024
TTT ID #:	2023-4843-2 and 2024-8044-1
DMEPA 1 Safety Evaluator:	Madhuri R. Patel, PharmD
DMEPA 1 Team Leader:	Yevgeniya Kogan, PharmD, BCSCP

[a] The non-proprietary name suffix for this product has not yet been determined; therefore, the placeholder established name-ttwe is used throughout this review to refer to the non-proprietary name and suffix for this product.

1 PURPOSE OF MEMORANDUM

Samsung Bioepis Co., LTD submitted revised container label and carton labeling received on May 22, 2024 for Pyzchiva. The Division of Dermatology and Dentistry (DDD) requested that we review the revised container label and carton labeling for Pyzchiva (Appendix A) to determine if they are acceptable from a medication error perspective. The revisions are in response to recommendations that we made during a previous label and labeling review.[b]

2 CONCLUSION

The container label and carton labeling are unacceptable from a medication error perspective. We note the font color used for the non-proprietary name for the 90 mg/mL has been revised to a (b) (4) color (b) (4) (b) (4) Additionally, the (b) (4) color used for the 90 mg/mL strength differentiation continues to overlap with the (b) (4) color used for the nonproprietary name for the 45 mg/0.5 mL and 130 mg/26 mL (5 mg/mL) strength carton and container.

3 RECOMMENDATIONS FOR SAMSUNG BIOEPIS CO., LTD

A. General Comments (Container Label(s) & Carton Labeling)

1. We note the font color used for the non-proprietary name for the 90 mg/mL has been revised to a (b) (4) color. (b) (4) Additionally, the 90 mg/mL strength is not clearly differentiated due to the similarity between the (b) (4) color which also overlap with the font color used for the non-proprietary name for the 45 mg/0.5 mL and 130 mg/26 mL (5 mg/mL) strength. Lack of adequate differentiation may contribute to wrong strength errors. Color differentiation is most effective when the color used has no association with a particular feature and there is no pattern in the application of the color scheme. We continue to recommend revising the color scheme of the 90 mg/mL strength and non-proprietary name such that all three strengths appear in their own unique colors that also do not overlap with the color used for the non-proprietary name for other strengths.

2 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

[b] Patel, M. Label and Labeling Review Memo for Pyzchiva (BLA 761373 and BLA 761425). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2024 APR 30. TTT ID: 2023-4843-1 and 2024-8044.

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MADHURI R PATEL
06/03/2024 08:58:49 AM

YEVGENIYA M KOGAN
06/03/2024 04:28:30 PM

MEMORANDUM
REVIEW OF REVISED LABEL AND LABELING

Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

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Date of This Review:	April 30, 2024
Requesting Office or Division:	Division of Dermatology and Dentistry (DDD)
Application Type and Number:	BLA 761373 and BLA 761425
Product Name, Dosage Form, and Strength:	Pyzchiva (ustekinumab-ttwe)[a] injection, 45 mg/0.5 mL and 90 mg/mL prefilled syringe and 130 mg/26 mL (5 mg/mL) vial
Applicant Name:	Samsung Bioepis Co., Ltd
FDA Received Date:	March 19, 2024, March 20, 2024, and April 10, 2024
TTT ID #:	2023-4843-1 and 2024-8044
DMEPA 1 Safety Evaluator:	Madhuri R. Patel, PharmD
DMEPA 1 Team Leader:	Yevgeniya Kogan, PharmD, BCSCP

[a] The non-proprietary name suffix for this product has not yet been determined for BLA 761425; therefore, the placeholder ustekinumab-ttwe is used throughout this review to refer to the non-proprietary name and suffix for this product.

1 PURPOSE OF MEMORANDUM

Samsung Bioepis Co., Ltd submitted revised container labels and carton labeling received on March 19, 2024 (BLA 761373) and on March 20, 2024 (BLA 761425) and revised Prescribing Information (PI), Medication Guide (MG), Instructions for Use (IFU) on April 10, 2024 (BLA 761373 and BLA 761425) and for Pyzchiva. The Division of Dermatology and Dentistry (DDD) requested that we review the revised container labels and carton labeling for Pyzchiva (Appendix A) to determine if they are acceptable from a medication error perspective. The revisions are in response to recommendations that we made during a previous label and labeling review.[b] We previously reviewed the PI, MG, IFU, container labels and carton labeling under BLA 761373 for the 45 mg/0.5 mL and 90 mg/mL prefilled syringes and 130 mg/26 mL (5 mg/mL) vial. However, since then, Samsung Bioepis Co., Ltd submitted BLA 761425 which is intended to be specifically for the 130 mg/26 mL (5 mg/mL) vial used for the initial intravenous dose for Crohn's Disease (CD) and Ulcerative Colitis (UC), whereas the 45 mg/0.5 mL and 90 mg/mL prefilled syringe presentations will remain under BLA 761373.

2 CONCLUSION

The container labels and carton labeling are unacceptable from a medication error perspective. We note the color scheme for the revised container labels and carton labeling have been revised. However, the color scheme of the 90 mg/mL strength (b) (4) (b) (4)

3 RECOMMENDATIONS FOR SAMSUNG BIOEPIS CO., LTD

A. General Comments (Container Label(s) & Carton Labeling)

1. The 90 mg/mL strength is not clearly differentiated due to the similarity between the (b) (4) color (b) (4) (b) (4) Lack of adequate differentiation may contribute to wrong strength errors. Color differentiation is most effective when the color used has no association with a particular feature and there is no pattern in the application of the color scheme. We recommend revising the color scheme of the 90 mg/mL strength (b) (4) such that the strengths (b) (4) (b) (4) appear in their own unique colors (b) (4)

[b] Patel, M. Label and Labeling Review for Pyzchiva (BLA 761373). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2023 DEC 18. TTT ID: 2023-4843.

APPENDIX A. LABELS AND LABELING

A.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,[c] along with postmarket medication error data, we reviewed the following Pyzchiva labels and labeling submitted by Samsung Bioepis Co., Ltd.

- Prescribing Information, Medication Guide, and Instructions for Use received on April 10, 2024, available from \\CDSESUB1\EVSPROD\bla761373\0041\m1\us\114-labeling\114a-draft-label\sb17_bla-761373-pi-ppi-ifu-20240409_v0-11_tracked.docx and \\CDSESUB1\EVSPROD\bla761425\0005\m1\us\114-labeling\114a-draft-label\sb17_bla-761425-pi-ppi-ifu-20240409_v0-11_tracked.docx
- Container label(s) received on March 19, 2024 and March 20, 2024
- Carton labeling received on March 19, 2024 and March 20, 2024

A.2 Container Label(s) and Carton Labeling Images

Container Label(s)

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[c] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

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MADHURI R PATEL
04/30/2024 10:55:46 AM

YEVGENIYA M KOGAN
04/30/2024 02:32:09 PM

LABEL AND LABELING REVIEW
Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

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Date of This Review:	December 18, 2023
Requesting Office or Division:	Division of Dermatology and Dentistry (DDD)
Application Type and Number:	BLA 761373
Product Name, Dosage Form, and Strength:	Pyzchiva (ustekinumab-xxxx)[a] injection, 45 mg/0.5 mL and 90 mg/mL prefilled syringe and 130 mg/26 mL (5 mg/mL) vial
Product Type:	Combination Product (Biologic-Device)
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Samsung Bioepis Co., Ltd.
FDA Received Date:	March 30, 2023 and November 27, 2023
TTT ID #:	2023-4843
DMEPA 1 Acting Team Leader:	Madhuri R. Patel, PharmD
DMEPA 1 Team Leader:	Yevgeniya Kogan, PharmD, BCSCP

[a] The nonproprietary name for this BLA has not yet been determined; therefore, the placeholder "ustekinumab-xxxx" is used throughout this review to refer to the non-proprietary name for this product and not intended to be included in the final labels and labeling.

1 REASON FOR REVIEW

As part of the approval process for Pyzchiva (ustekinumab-xxxx) injection, the Division of Dermatology and Dentistry (DDD) requested that we review the proposed Pyzchiva Prescribing Information (PI), Medication Guide (MG), Instructions for Use (IFU), container labels and carton labeling for areas of vulnerability that may lead to medication errors.

2 MATERIALS REVIEWED

Table 1. Materials Considered for this Label and Labeling Review

Material Reviewed	Appendix Section (for Methods and Results)
Product Information/Prescribing Information	A
Previous DMEPA Reviews	B – N/A
ISMP Newsletters*	C – N/A
FDA Adverse Event Reporting System (FAERS)*	D – N/A
Other	E – N/A
Labels and Labeling	F

N/A=not applicable for this review
*We do not typically search FAERS or ISMP Newsletters for our label and labeling reviews unless we are aware of medication errors through our routine postmarket safety surveillance

3 CONCLUSION AND RECOMMENDATIONS

The proposed Prescribing Information (PI), Medication Guide (MG), Instructions for Use (IFU), container labels and carton labeling may be improved to promote the safe use of this product from a medication error perspective. Note that DMEPA 1 is evaluating the human factors (HF) data under separate cover and based on the outcome of that review, additional label and labeling comments may be forthcoming. We provide the identified medication error issues, our rationale for concern, and our proposed recommendations to minimize the risk for medication error in Section 4 for the Division and in Section 5 for Samsung Bioepis Co., Ltd..

4 RECOMMEDATIONS FOR DIVISION OF DERMATOLOGY AND DENTISTRY (DDD)

Table 2. Identified Issues and Recommendations for Division of Dermatology and Dentistry (DDD)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Prescribing Information (PI), Medication Guide (MG), and Instructions for Use (IFU) – General Issues			
1.	As currently presented, the proprietary name is denoted by the placeholder "SB17".	The proprietary name "Pyzchiva" was found conditionally acceptable under OSE PNR ID# 2023-1044725066 on June 14, 2023.	Replace the placeholder "SB17" in the PI, MG, and IFU with the conditionally acceptable proprietary name "Pyzchiva".
2.	The nonproprietary name suffix is denoted by the placeholder '-xxxx'.	A distinguishable nonproprietary name will facilitate accurate identification of the biological product by healthcare providers and patients.	Replace '-xxxx' with the conditionally acceptable nonproprietary name suffix when it is determined.

5 RECOMMENDATIONS FOR SAMSUNG BIOEPIS CO., LTD.

Table 3. Identified Issues and Recommendations for Samsung Bioepis Co., Ltd. (entire table to be conveyed to Applicant) Note that additional label and labeling comments may be forthcoming when we have completed our evaluation of your human factors (HF) data.			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Container Label(s) and Carton Labeling			
1.	As currently presented, the proprietary name is denoted by the placeholder "SB17".	We are unable to assess the prominence and readability of the intended presentation of the proprietary name.	We reference our June 20, 2023 Proprietary Name Request Conditionally Acceptable letter informing you that the proprietary name, Pyzchiva, was found conditionally acceptable. We recommend replacing the placeholder "SB17" with the conditionally acceptable proprietary name, Pyzchiva, and use the intend-to-market presentation of the proprietary

Table 3. Identified Issues and Recommendations for Samsung Bioepis Co., Ltd. (entire table to be conveyed to Applicant) Note that additional label and labeling comments may be forthcoming when we have completed our evaluation of your human factors (HF) data.			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
			name (font, color, etc.) so that we may adequately evaluate your labels and labeling.
2.	As currently presented, the placeholder 'xxxx' for the suffix is present as part of the nonproprietary name on the principal display panel.	A distinguishable nonproprietary name will facilitate accurate identification of the biological product by healthcare providers and patients.	Once a nonproprietary name is found conditionally acceptable for your proposed product, revise the nonproprietary name on all labels and labeling to incorporate the FDA-designated nonproprietary name suffix throughout the labels and labeling.
3.	The 90 mg/mL strength is not clearly differentiated due to the similarity between the (b) (4) colors which also overlap with the font colors used for the non-proprietary name.	Lack of adequate differentiation may contribute to wrong strength errors. Color differentiation is most effective when the color used has no association with a particular feature and there is no pattern in the application of the color scheme.	We recommend revising the color scheme of the 90 mg/mL strength or non-proprietary name such that the strengths and the non-proprietary name appear in their own unique colors that do not overlap.
4.	As currently presented, the format for the expiration date is not defined.	We are unable to assess the proposed expiration date format from a medication safety perspective.	To minimize confusion and reduce the risk for deteriorated drug medication errors, we recommend identifying the expiration date format you intend to use. FDA recommends that the human-readable expiration date on the drug package label include a year, month, and non-zero day. FDA recommends that the expiration date appear in YYYY-MM-DD format if only numerical characters are used

Table 3. Identified Issues and Recommendations for Samsung Bioepis Co., Ltd. (entire table to be conveyed to Applicant) Note that additional label and labeling comments may be forthcoming when we have completed our evaluation of your human factors (HF) data.			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
			or in YYYY-MMM-DD if alphabetical characters are used to represent the month. If there are space limitations on the drug package, the human-readable text may include only a year and month, to be expressed as: YYYY-MM if only numerical characters are used or YYYY-MMM if alphabetical characters are used to represent the month. FDA recommends that a hyphen or forward slash to separate the portions of the expiration date. See *Guidance for Industry: Product Identifiers under the Drug Supply Chain Security Act - Questions and Answers (June 2021).*
Container Label(s)			
1.	For the 130 mg/26 mL vial, the principal display panel (PDP) is displaying duplicate strength presentations.	When the container labels are crowded, text size and prominence are generally decreased, and important information may be difficult to read or easily overlooked.	We recommend removing the product strength presentation from the top right portion of the PDP. Incorporate boxing or highlighting to increase the prominence of the product strength statement that appears under the dosage formulation, injection.
Carton Labeling			
1.	The net quantity statement does not appear on the principal display panel of the vial carton labeling.	Failure to include the net quantity statement on the principal display panel may result in confusion regarding the contents of the carton.	We recommend revising the statement “Single-dose vial” on the principal display panel include a net quantity statement [e.g., ‘One single-dose vial’ or ‘1 single-dose vial’]

Table 3. Identified Issues and Recommendations for Samsung Bioepis Co., Ltd. (entire table to be conveyed to Applicant) Note that additional label and labeling comments may be forthcoming when we have completed our evaluation of your human factors (HF) data.			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
			on the principal display panel and ensure it is located away from and less prominent than the product strength. *See Guidance for Industry: Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors (May 2022).*
2.	The product identifier is missing.	In June 2021, FDA finalized the Guidance for Industry on product identifiers required under the Drug Supply Chain Security Act (DSCSA). The Act requires manufacturers and re-packagers to affix or imprint a product identifier to each package and homogenous case of a product intended to be introduced in a transaction in(to) commerce. The product identifier includes the NDC, serial number, lot number, and expiration date in both a human-readable form and machine-readable (2D data matrix barcode) format.	We recommend that you review the guidance to determine if the product identifier requirements apply to your product's labeling. See Guidance for Industry: Product Identifiers under the Drug Supply Chain Security Act - Questions and Answers (June 2021). If you determine that the product identifier requirements apply to your product's labeling, we request you add a place holder to the carton labeling.
3.	For the prefilled syringe carton labeling, the terminology within the statement of dosage statement "(b) (4) is inconsistent with the	To ensure consistency with the terminology in the Prescribing Information.	We recommend revising the statement of dosage statement to read, "Recommended Dosage: see Prescribing Information."

Table 3. Identified Issues and Recommendations for Samsung Bioepis Co., Ltd. (entire table to be conveyed to Applicant) Note that additional label and labeling comments may be forthcoming when we have completed our evaluation of your human factors (HF) data.			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
	terminology in the Prescribing Information.		

APPENDICES: METHODS & RESULTS FOR EACH MATERIAL REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table presents relevant product information for Pyzchiva that Samsung Bioepis Co., Ltd. submitted on November 27, 2023, and Stelara.

Table 4. Relevant Product Information for Listed Drug and Pyzchiva		
Product Name	Stelara[b]	Pyzchiva
Initial Approval Date	September 25, 2009 (BLA 125261) September 23, 2016 (BLA 761044)	N/A
Active Ingredient	ustekinumab	ustekinumab-xxxx
Indication	Psoriasis (Ps) treatment of patients 6 years or older with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy. Psoriatic Arthritis (PsA) treatment of patients 6 years or older with active psoriatic arthritis. Crohn's Disease (CD) treatment of adult patients with moderately to severely active Crohn's disease. Ulcerative Colitis treatment of adult patients with moderately to severely active ulcerative colitis.	
Route of Administration	subcutaneous, intravenous	
Dosage Form	injection	

[b] Stelara [Prescribing Information]. Drugs@FDA. U.S. Food and Drug Administration. 2023 MAR 06. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/125261s158lbl.pdf.

Table 4. Relevant Product Information for Listed Drug and Pyzchiva		
Product Name	Stelara[b]	Pyzchiva
Strength	Subcutaneous: Prefilled syringe: 45 mg/0.5 mL, 90 mg/mL Vial: 45 mg/0.5 mL Intravenous: 130 mg/26 mL (5 mg/mL)	Subcutaneous: Prefilled syringe: 45 mg/0.5 mL, 90 mg/mL Intravenous: 130 mg/26 mL (5 mg/mL)

<table>
<tr><th colspan="3">Table 4. Relevant Product Information for Listed Drug and Pyzchiva</th></tr>
<tr><td>Product Name</td><td>Stelara[b]</td><td>Pyzchiva</td></tr>
<tr><td>Dose and Frequency</td><td>Psoriasis (Ps)
<u>Subcutaneous Adult:</u>
• For patients weighing 100 kg or less, the recommended dose is 45 mg initially and 4 weeks later, followed by 45 mg every 12 weeks.
• For patients weighing more than 100 kg, the recommended dose is 90 mg initially and 4 weeks later, followed by 90 mg every 12 weeks.
In subjects weighing more than 100 kg, 45 mg was also shown to be efficacious. However, 90 mg resulted in greater efficacy in these subjects
<u>Subcutaneous Pediatric:</u>
Administer subcutaneously at Weeks 0 and 4, then every 12 weeks thereafter.
The recommended dose for pediatric patients (6-17 years old) based on body weight is shown below.
<table><tr><th>Body Weight of Patient at the Time of Dosing</th><th>Recommended Dose</th></tr><tr><td>less than 60 kg*</td><td>0.75 mg/kg</td></tr><tr><td>60 kg to 100 kg</td><td>45 mg</td></tr><tr><td>more than 100 kg</td><td>90 mg</td></tr></table>*For pediatric patients weighing less than 60 kg… withdraw the appropriate volume from the single-dose vial.</td><td>Psoriasis (Ps)
<u>Subcutaneous Adult:</u>
• For patients weighing 100 kg or less, the recommended dose is 45 mg initially and 4 weeks later, followed by 45 mg every 12 weeks.
• For patients weighing more than 100 kg, the recommended dose is 90 mg initially and 4 weeks later, followed by 90 mg every 12 weeks.
In subjects weighing more than 100 kg, 45 mg was also shown to be efficacious. However, 90 mg resulted in greater efficacy in these subjects
<u>Subcutaneous Pediatric:</u>
Administer subcutaneously at Weeks 0 and 4, then every 12 weeks thereafter.
The recommended dose for pediatric patients (6-17 years old) based on body weight is shown below.
<table><tr><th>Body Weight of Patient at the Time of Dosing</th><th>Recommended Dose</th></tr><tr><td>60 kg to 100 kg</td><td>45 mg</td></tr><tr><td>more than 100 kg</td><td>90 mg</td></tr></table>Note: There is no dosage form for SB17 that allows weight base dosing for pediatric patients below 60 kg (132 pounds). (b) (4) [redacted]</td></tr>
</table>

<table>
<tr><th colspan="3">Table 4. Relevant Product Information for Listed Drug and Pyzchiva</th></tr>
<tr><td>Product Name</td><td>Stelara[b]</td><td>Pyzchiva</td></tr>
<tr><td></td><td>Psoriatic Arthritis (PsA)
<u>Subcutaneous Adult:</u>
• The recommended dose is 45 mg initially and 4 weeks later, followed by 45 mg every 12 weeks.
• For patients with co-existent moderate-to-severe plaque psoriasis weighing more than 100 kg, the recommended dose is 90 mg initially and 4 weeks later, followed by 90 mg every 12 weeks.
<u>Subcutaneous Pediatric:</u>
Administer subcutaneously at Weeks 0 and 4, then every 12 weeks thereafter.
The recommended dose for pediatric patients (6-17 years old) based on body weight is shown below.
<table>
<tr><th>Body Weight of Patient at the Time of Dosing</th><th>Recommended Dose</th></tr>
<tr><td>less than 60 kg*</td><td>0.75 mg/kg</td></tr>
<tr><td>60 kg or more</td><td>45 mg</td></tr>
<tr><td>greater than 100 kg with co-existent moderate-to-severe plaque psoriasis</td><td>90 mg</td></tr>
</table>
*For pediatric patients weighing less than 60 kg… withdraw the appropriate volume from the single-dose vial.</td><td>Psoriatic Arthritis (PsA)
<u>Subcutaneous Adult:</u>
• The recommended dose is 45 mg initially and 4 weeks later, followed by 45 mg every 12 weeks.
• For patients with co-existent moderate-to-severe plaque psoriasis weighing more than 100 kg, the recommended dose is 90 mg initially and 4 weeks later, followed by 90 mg every 12 weeks.
<u>Subcutaneous Pediatric:</u>
Administer subcutaneously at Weeks 0 and 4, then every 12 weeks thereafter.
The recommended dose for pediatric patients (6-17 years old) based on body weight is shown below.
<table>
<tr><th>Body Weight of Patient at the Time of Dosing</th><th>Recommended Dose</th></tr>
<tr><td>60 kg or more</td><td>45 mg</td></tr>
<tr><td>greater than 100 kg with co-existent moderate-to-severe plaque psoriasis</td><td>90 mg</td></tr>
</table>
Note: There is no dosage form for SB17 that allows weight base dosing for pediatric patients below 60 kg (132 pounds). (b) (4)</td></tr>
</table>

<table>
<tr><td colspan="3">Table 4. Relevant Product Information for Listed Drug and Pyzchiva</td></tr>
<tr><td>Product Name</td><td>Stelara[b]</td><td>Pyzchiva</td></tr>
<tr><td></td><td>Crohn's Disease (CD) and Ulcerative Colitis
<u>Intravenous Induction Adult</u>:
A single intravenous infusion dose using the weight-based dosage regimen.
<table>
<tr><th>Body Weight of Patient at the time of dosing</th><th>Dose</th><th>Number of 130 mg/26 mL (5 mg/mL) vials</th></tr>
<tr><td>55 kg or less</td><td>260 mg</td><td>2</td></tr>
<tr><td>more than 55 kg to 85 kg</td><td>390 mg</td><td>3</td></tr>
<tr><td>more than 85 kg</td><td>520 mg</td><td>4</td></tr>
</table>
<u>Subcutaneous Maintenance Adult</u>:
The recommended maintenance dosage is a subcutaneous 90 mg dose administered 8 weeks after the initial intravenous dose, then every 8 weeks thereafter.</td><td>Crohn's Disease (CD) and Ulcerative Colitis
<u>Intravenous Induction Adult</u>:
A single intravenous infusion dose using the weight-based dosage regimen.
<table>
<tr><th>Body Weight of Patient at the time of dosing</th><th>Dose</th><th>Number of 130 mg/26 mL (5 mg/mL) vials</th></tr>
<tr><td>55 kg or less</td><td>260 mg</td><td>2</td></tr>
<tr><td>more than 55 kg to 85 kg</td><td>390 mg</td><td>3</td></tr>
<tr><td>more than 85 kg</td><td>520 mg</td><td>4</td></tr>
</table>
<u>Subcutaneous Maintenance Adult</u>:
The recommended maintenance dosage is a subcutaneous 90 mg dose administered 8 weeks after the initial intravenous dose, then every 8 weeks thereafter.</td></tr>
</table>

Table 4. Relevant Product Information for Listed Drug and Pyzchiva		
Product Name	**Stelara[b]**	Pyzchiva
How Supplied	sterile, preservative-free, colorless to light yellow solution and may contain a few small translucent or white particles. It is supplied as individually packaged, single-dose prefilled syringes or single-dose vials <u>For Subcutaneous Use</u> *Prefilled Syringes* • 45 mg/0.5 mL (NDC 57894-060-03) • 90 mg/mL (NDC 57894-061-03) Each prefilled syringe is equipped with a 27 gauge fixed ½ inch needle, a needle safety guard, and a needle cover that contains dry natural rubber. *Single-dose Vial* • 45 mg/0.5 mL (NDC 57894-060-02) <u>For Intravenous Infusion</u> *Single-dose Vial* • 130 mg/26 mL (5 mg/mL) (NDC 57894-054-27)	clear, colorless to light yellow, sterile and preservative-free solution. It is supplied as individually packaged, single-dose prefilled syringes or single-dose vials <u>For Subcutaneous Use</u> *Prefilled Syringes* • 45 mg/0.5 mL (NDC XXXXX-XXX-XX) • 90 mg/mL (NDC XXXXX-XXX-XX) Each prefilled syringe is equipped with a 29 gauge fixed ½ inch needle, a needle safety guard, and a needle cover that (b) (4) <u>For Intravenous Infusion</u> *Single-dose Vial* • 130 mg/26 mL (5 mg/mL) (NDC XXXXX-XXX-XX)

Table 4. Relevant Product Information for Listed Drug and Pyzchiva		
Product Name	**Stelara[b]**	Pyzchiva
Storage	vials and prefilled syringes must be refrigerated at 2°C to 8°C (36°F to 46°F). Store vials upright. Keep the product in the original carton to protect from light until the time of use. Do not freeze. Do not shake. If needed, individual prefilled syringes may be stored at room temperature up to 30°C (86°F) for a maximum single period of up to 30 days in the original carton to protect from light. Record the date when the prefilled syringe is first removed from the refrigerator on the carton in the space provided. Once a syringe has been stored at room temperature, it should not be returned to the refrigerator. Discard the syringe if not used within 30 days at room temperature storage. Do not use after the expiration date on the carton or on the prefilled syringe.	vials and prefilled syringes must be refrigerated at 2°C to 8°C (36°F to 46°F). Store vials upright. Keep the product in the original carton to protect from light until the time of use. Do not freeze. Do not shake. If needed, individual prefilled syringes may be (b) (4) stored at room temperature up to 30°C (86°F) for a maximum single period of up to 60 days in the original carton to protect from light. Record the date when the prefilled syringe is (b) (4) Do not use SB17 after the expiration date on the carton or on the prefilled syringe
Container Closure	Prefilled Syringe: Each prefilled syringe is equipped with a 27 gauge fixed ½ inch needle, a needle safety guard, and a needle cover that contains dry natural rubber Vial: N/A	Prefilled Syringe: Each prefilled syringe is equipped with a 29 gauge fixed ½ inch needle, a needle safety guard, and a needle cover that (b) (4) (b) (4) Vial: N/A

APPENDIX F. LABELS AND LABELING

F.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,[c] along with postmarket medication error experiences with similar products, we reviewed the following Pyzchiva labels and labeling submitted by Samsung Bioepis Co., Ltd..

- Container Labels received on March 30, 2023
- Carton Labeling received on March 30, 2023
- Professional Sample Container Labels received on March 30, 2023
- Professional Sample Carton Labeling received on March 30, 2023
- Prescribing Information, Medication Guide, and Instructions for Use (Images not shown) received on November 27, 2023, available from \\CDSESUB1\EVSPROD\bla761373\0023\m1\us\114-labeling\114a-draft-label\uspi-v0-6-redline.pdf

F.2 Label and Labeling Images

Container label(s)

(b) (4)

[c] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

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/s/

MADHURI R PATEL
12/19/2023 10:41:17 AM

YEVGENIYA M KOGAN
12/20/2023 08:55:53 AM

FOOD AND DRUG ADMINISTRATION
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion

****Pre-decisional Agency Information****

Memorandum

Date: 12/14/2023

To: Strother D. Dixon, RPM, Division of Dermatology and Dentistry (DDD)

Shera C. Schreiber, Clinical Reviewer

Matthew White, Associate Director for Labeling

From: Montherson L Saint Juste, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: James Dvorsky, Team Leader, OPDP

Subject: OPDP Labeling Comments for SB17 (ustekinumab-xxxx) injection, for subcutaneous or intravenous

BLA: 761373

Background:
In response to DDD's consult request dated May 26, 2023, OPDP has reviewed the proposed Prescribing Information (PI), Medication Guide, Instructions for Use (IFU), for the original BLA submission for SB17 (ustekinumab-xxxx) injection.

PI/Medication Guide/IFU:
OPDP's review of the proposed PI is based on the draft labeling emailed to OPDP on November 21, 2023, and we do not have any comments at this time.

A combined OPDP and Division of Medical Policy Programs (DMPP) review was completed for the proposed Medication Guide and IFU, and comments were sent under separate on December 13, 2023.

Carton and Container Labeling:
OPDP's review of the proposed carton and container labeling is based on the draft labeling submitted by the sponsor to the electronic document room on March 30, 2023, and we do not have any comments at this time.

Thank you for your consult. If you have any questions, please contact Montherson L. Saint Juste at Montherson.SaintJuste@fda.hhs.gov.

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/s/

JAMES S DVORSKY on behalf of MONTHERSON L SAINT JUSTE
12/14/2023 11:04:29 AM

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Medical Policy

PATIENT LABELING REVIEW

Date:	December 13, 2023
To:	Strother D. Dixon, PharmD Senior Regulatory Project Manager **Division of Dermatology and Dentistry (DDD)**
Through:	LaShawn Griffiths, MSHS-PH, BSN, RN Associate Director for Patient Labeling **Division of Medical Policy Programs (DMPP)**
From:	Laurie Buonaccorsi, PharmD Senior Patient Labeling Reviewer **Division of Medical Policy Programs (DMPP)** Montherson L. Saint Juste, PharmD, MS Regulatory Review Officer **Office of Prescription Drug Promotion (OPDP)**
Subject:	Review of Patient Labeling: Medication Guide (MG) and Instructions for Use (IFU)
Drug Name (nonproprietary name); Dosage Form and Route:	[SB17] PYZCHIVA (ustekinumab-xxxx)[1] injection, for subcutaneous or intravenous use • subcutaneous injection, 45 mg/0.5 mL or 90 mg/mL in a single-dose prefilled syringe • intravenous infusion, 130 mg/26 mL (5 mg/mL) in a single-dose vial
Application Type/Number:	BLA 761373
Applicant:	Samsung Bioepis Co., Ltd. c/o ICON Clinical Research, LLC

[1] SB17 was developed as a proposed biosimilar to US-licensed Stelara (ustekinumab) BLA 125261 and BLA 761044. The proposed Tradename PYZCHIVA was found to be conditionally acceptable by the Division of Medication Error Prevention and Analysis I (DMEPA 1) on June 20, 2023. The nonproprietary name suffix has not been determined at this time and we therefore use the placeholder "-xxxx" for the 4-letter nonproprietary name suffix.

1 INTRODUCTION

On March 30, 2023, Samsung Bioepis Co., Ltd. c/o ICON Clinical Research, LLC submitted for the Agency's review an original Biologics License Application (BLA) 761373 for [SB17] PYZCHIVA (ustekinumab-xxxx) injection, a proposed interchangeable biosimilar to US-licensed STELARA (ustekinumab) injection [BLA 125261 and BLA 761044] for the treatment of the following:

- patients 6 years or older with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy
- patients 6 years or older with active psoriatic arthritis
- adults with moderately to severely active Crohn's Disease
- adults with moderately to severely active ulcerative Colitis

This collaborative review is written by the Division of Medical Policy Programs (DMPP) and the Office of Prescription Drug Promotion (OPDP) in response to a request by the Division of Dermatology and Dentistry (DDD) on May 26, 2023, for DMPP and OPDP to review the Applicant's proposed Medication Guide (MG) and Instructions for Use (IFU) for [SB17] PYZCHIVA (ustekinumab-xxxx) injection.

DMPP conferred with the Division of Medication Error, Prevention, and Analysis (DMEPA) and a separate DMEPA review of the IFU will be forthcoming.

2 MATERIAL REVIEWED

- Draft [SB17] PYZCHIVA (ustekinumab-xxxx) injection MG received on March 30, 2023, revised by the Review Division throughout the review cycle, and received by DMPP on November 22, 2023.
- Draft [SB17] PYZCHIVA (ustekinumab-xxxx) injection single-dose prefilled syringe IFU, received on March 30, 2023, revised by the Review Division throughout the review cycle, and received by DMPP on November 22, 2023.
- Draft [SB17] PYZCHIVA (ustekinumab-xxxx) injection Prescribing Information (PI) received on March 30, 2023, revised by the Review Division throughout the review cycle, and received by DMPP on November 22, 2023.
- Approved US-licensed STELARA (ustekinumab) injection MG dated March 6, 2023, and IFU dated April 6, 2020.

3 REVIEW METHODS

To enhance patient comprehension, materials should be written at a 6th to 8th grade reading level, and have a reading ease score of at least 60%. A reading ease score of 60% corresponds to an 8th grade reading level. In our review of the IFU, the target reading level is at or below an 8th grade level.

Additionally, in 2008 the American Society of Consultant Pharmacists Foundation (ASCP) in collaboration with the American Foundation for the Blind (AFB) published *Guidelines for Prescription Labeling and Consumer Medication Information for People with Vision Loss*. The ASCP and AFB recommended using

fonts such as Verdana, Arial or APHont to make medical information more accessible for patients with vision loss. We reformatted the MG and IFU documents using the Arial font, size 10.

In our collaborative review of the MG and IFU we:

- simplified wording and clarified concepts where possible
- ensured that the MG and IFU are consistent with the PI
- removed unnecessary or redundant information
- ensured that the MG and IFU are free of promotional language or suggested revisions to ensure that they are free of promotional language
- ensured that the MG meets the Regulations as specified in 21 CFR 208.20
- evaluated the MG and IFU per the criteria as specified in FDA's Guidance for Useful Written Consumer Medication Information (published July 2006)
- ensured that the MG and IFU are consistent with the approved labeling for US-licensed STELARA (ustekinumab) injection where applicable.

4 CONCLUSIONS

The MG and IFU are acceptable with our recommended changes.

5 RECOMMENDATIONS

- Please send these comments to the Applicant and copy DMPP and OPDP on the correspondence.
- Our collaborative review of the MG and IFU is appended to this memorandum. Consult DMPP and OPDP regarding any additional revisions made to the PI to determine if corresponding revisions need to be made to the MG and IFU.

Please let us know if you have any questions.

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/

LAURIE J BUONACCORSI
12/13/2023 03:05:57 PM

MONTHERSON L SAINT JUSTE
12/13/2023 03:24:39 PM

LASHAWN M GRIFFITHS
12/13/2023 04:51:20 PM