CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761258Orig1s000

OTHER REVIEW(S)

Addendum to Clinical Inspection Summary
Dated March 27, 2025

Date	April 21, 2025
From	Lee Pai-Scherf, MD Michele Fedowitz, MD, Team Leader Jenn Sellers, MD, PhD, Branch Chief Good Clinical Practice Assessment Branch (GCPAB) DCCE, OSI
To	Kevin Breen, Medical Officer Timil Patel, Medical Team Leader Paz Vellanki, Supervisory Associated Director Division of Oncology 2 (DO2), Office of Oncology Products
BLA #	BLA 761258 (Class 2 resubmission)
Applicant	Akeso Biopharma Co., Ltd
Drug	Penpulimab-kcqx
NME (Yes/No)	Yes
Therapeutic Classification	Programmed death receptor-1 (PD-1)-blocking antibody
Proposed Indication(s)	- In combination with gemcitabine and cisplatin or carboplatin as first-line treatment of patients with recurrent or metastatic nasopharyngeal carcinoma (NPC) - For the treatment of adults with metastatic non-keratinizing NPC with disease progression on or after platinum-based chemotherapy and at least one other prior line of therapy.
Consultation Request Date	November 20, 2024
Summary Goal Date	March 2, 2025 (extension to March 28, 2025)
Action Goal Date	April 2, 2025
PDUFA Date	April 2, 2025

This is an addendum to the Clinical Inspection Summary (CIS) for BLA 761258, dated March 27, 2025. The basis for this addendum is to provide an update of the review of the Establishment Inspection Reports (EIRs) that were not available at the time of the initial CIS for Drs. Feng Liu (Site # 1004), and Song Qu (Site # 1023), as well as the Sponsor, Akeso Biopharma Co., Ltd., and the imaging Contract Research Organization (CRO), (b) (4) (b) (4).

The initial CIS based on the summaries provided by the FDA field investigators indicated Study AK105-304 appears to have been conducted adequately and the data generated by the inspected clinical investigators and the imaging CRO and submitted by the Applicant appear acceptable in support of the proposed indication.

No significant new information was identified based on the review of the EIRs for Drs. Liu (Site # 1004), Qu (Site # 1023), and the imaging Contract Research Organization (CRO), (b) (4) (b) (4) that would impact on subject safety or data integrity.

During the sponsor inspection, an Akeso Biopharma sponsor representative reported 42 protocol deviations that hadn't been previously submitted to the BLA. Akeso stated that the deviations were identified after the study data cutoff date of April 29, 2024. These deviations have been since submitted to the review division via electronic mail on March 28, 2025, and to the BLA 761258 on April 17, 2025.

The protocol deviations occurred in a total of 29 subjects and are briefly summarized in Table 1 below by category:

Table 1. Protocol Deviations not previously Submitted to the BLA

Categories	N	Description (N)
Visit schedule	22	• Visit delayed by due to inability to reach hospital during COVID-19 pandemic (10) • Survival follow-up earlier/later than the planned date (8) • Subject refused to return for 30d end-of-treatment visit (2) • Subject refused open-label visit (1) • Subject unable to return for follow-up after Wk 99 (1)
Study procedures	7	• Laboratory samples not mailed according to manual (4) • Missed ECG examination (2) • Subject was not given QOL Questionnaire prior to a treatment cycle (1)
Efficacy criteria	5	• CT scans missed (1) or delayed* (5)
Laboratory Assessment	5	• Missed coagulation time test (2) • Extra blook samples collected for PK analysis (2) • Missed end of treatment laboratory tests (1)
Study drug compliance	1	• IP IV administration longer than protocol specified 60 +/- minutes by 16 minutes (1)
Safety reporting	1	• Failure to report SAE within 24 hours window (1)
Total	41**	

** See description below*
*** One additional subject (ID (b) (6)) had an unscheduled imaging scan performed on (b) (6), 7 days prior to Week 30 scan scheduled for (b) (6). Although the Sponsor reported this as a protocol deviation with 8-day delay, the scan was performed within the allowed window of +/- 7 days, therefore not included in the above table as a deviation.*

Reviewer Comment: The above protocol deviations do not appear to impact on patient safety. Delays in performing radiographic scans to assess efficacy occurred in 3 subjects in 5 time points and are summarized in Table 2.

Table 2. Efficacy Assessment Deviations

Subject ID	***Radiographic Assessment Planned Date***	***Deviation***	***Reason***
(b) (6)	*Week 6 -* (b) (6) *(+/-7 days)*	***Missed exam***	*COVID-19 pandemic*
	Week 24 - (b) (6) *(+/-7 days)*	*Delayed by **4 days***	*Adverse event*
	Week 24 - (b) (6) *(+/-7 days)*	*Delayed by **2 days***	-
	Week 30 - (+/-7 days)	*Delayed by **1 days***	-
	Week 12 - (+/-7 days)	*Delayed by **14 days***	*COVID-19 infection*

*Of note, **Subject** (b) (6) was randomized to the placebo plus chemotherapy arm and received the first dose of study treatment on (b) (6). The tumor assessment on Week 6 was not performed due to travel restrictions related to the COVID-19 pandemic. Subsequent tumor assessments on weeks 12, 18, 24 showed stable disease based on BICR review. The subject's tumor progressed on week 30. Thus, the missing Week 6 assessment does not seem to have an impact on the subject's overall response (Stable Disease).*

Subject (b) (6) *was randomized to the placebo plus chemotherapy arm and received the first dose of study treatment on (b) (6). Imaging scheduled for Week 12 was delayed by 14 days due to COVID-19 infection. However, scans conducted at Weeks 6 and 24 demonstrated stable disease per BICR, as did the delayed Week 12 scan. Therefore, the delay had not apparent impact on subject's overall efficacy assessment.*

Similarly radiographic assessments performed 1 to 4 days out of the scheduled window in the above other subjects are unlikely to alter the overall efficacy finds for study AK105-304.

Notwithstanding the unreported protocol deviations, Study AK105-304 appears to have been conducted adequately and the data generated by the inspected clinical investigators and the imaging CRO and submitted by the Applicant appear acceptable in support of the proposed indication.

{See appended electronic signature page}

Lee Pai-Scherf, MD
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Office of Scientific Investigations

CONCURRENCE:

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CONCURRENCE: {*See appended electronic signature page}*

Jenn Sellers, M.D., Ph.D.
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CC:

Review Division /Project Manager/Aisida Bamidele
OSI/DCCE/GCPAB/Program Analyst/Yolanda Patague

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/s/

LEE HONG PAI SCHERF
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MICHELE B FEDOWITZ
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JENN W SELLERS
04/21/2025 02:17:36 PM

Clinical Inspection Summary

Date	March 27, 2025
From	Lee Pai-Scherf, MD Michele Fedowitz, MD, Team Leader Jenn Sellers, MD, PhD, Branch Chief Good Clinical Practice Assessment Branch (GCPAB) DCCE, OSI
To	Kevin Breen, Medical Officer Timil Patel, Medical Team Leader Paz Vellanki, Supervisory Associated Director Division of Oncology 2 (DO2), Office of Oncology Products
BLA #	BLA 761258 (Class 2 resubmission)
Applicant	Akeso Biopharma Co., Ltd
Drug	Penpulimab-kcqx
NME (Yes/No)	Yes
Therapeutic Classification	Programmed death receptor-1 (PD-1)-blocking antibody
Proposed Indication(s)	- In combination with gemcitabine and cisplatin or carboplatin as first-line treatment of patients with recurrent or metastatic nasopharyngeal carcinoma (NPC) - For the treatment of adults with metastatic non-keratinizing NPC with disease progression on or after platinum-based chemotherapy and at least one other prior line of therapy.
Consultation Request Date	November 20, 2024
Summary Goal Date	March 2, 2025 (extension to March 28, 2025)
Action Goal Date	April 2, 2025
PDUFA Date	April 2, 2025

I. OVERALL ASSESSMENT OF FINDINGS AND RECOMMENDATIONS

Clinical data from Study AK105-304 were submitted to the Agency in support of Biologics License Application (BLA) 761258 for penpulimab in combination with gemcitabine and cisplatin or carboplatin as first-line treatment of patients with recurrent or metastatic nasopharyngeal carcinoma (NPC). Three clinical investigators (CI), Drs. Feng Liu (Site # 1004), Chuanben Chen (Site # 1007), and Song Qu (Site # 1023), as well as the Sponsor, Akeso Biopharma Co., Ltd. (heretofore Akeso) and the imaging Contract Research Organization (CRO), (b) (4) were inspected.

The inspections of Drs. Chen and Qu, the Sponsor, Akeso and the imaging CRO, (b) (4)

(b) (4) did not find significant concerns regarding the study conduct, data discrepancies or integrity, Good Clinical Practice (GCP), or regulatory compliance. The inspection of Dr. Liu observed that one tumor MRI scan of one subject (control group) at Week 56 of the study was not submitted for central review (see **Results**, below), which was assessed by the local radiologist as stable disease. The same subject had two previous scans at Week 42 and Week 48 that were assessed by the Blinded Independent Committee Review (BICR) as per protocol, which showed stable disease. OSI does not believe the protocol deviation of failure to submit one single tumor scan for central review would have a significant impact on the primary efficacy endpoint, however, OSI defers to the review division to consider its impact on overall study outcome, and censor as appropriate.

Based on these inspections, Study AK105-304 appears to have been conducted adequately and the data generated by the inspected clinical investigators and the imaging CRO and submitted by the Applicant appear acceptable in support of the proposed indication.

Of note, the inspection results of Drs. Liu, Qu, the Sponsor, Akeso and the imaging CRO, (b) (4) are based on summaries provided by the FDA field investigators and are therefore preliminary. If significantly new or different information is contained in the final FDA Establishment Inspection Reports, an addendum to this clinical inspection summary will be filed.

II. BACKGROUND

Akeso BioPharma Ltd submitted this Class 2 resubmission under BLA 761258 in response to the Complete Response (CR) letter issued by the FDA on January 19, 2024. The complete response was due to clinical deficiencies related to the changing treatment landscape for NPC and product quality deficiencies. The initial BLA, submitted in July 2021, contained data from a single arm study **AK105-202** to support an indication for penpulimab for the treatment of patients with NPC who had failed prior therapy. Inspections of three clinical investigators located in China, Drs. Jingao Li, Qingfeng Zou, Xiaozhong Chen, and the imaging CRO, (b) (4) were conducted, and did not reveal significant findings. The inspections were significantly delayed at the time due to the ongoing COVID-19 pandemic. Inspection of the Sponsor, Akeso Biopharma, was cancelled at the request of the review division before the CR letter was issued.

This submission seeks approval for penpulimab in combination with gemcitabine and cisplatin or carboplatin as first-line treatment of patients with recurrent or metastatic NPC, and for the treatment of adults with metastatic non-keratinizing NPC with disease progression on or after platinum-base chemotherapy and at least one other prior line of therapy.

The current submission contains clinical data from **Study AK105-304**, a randomized, double-blind study of chemotherapy in combination with either penpulimab or placebo to

support the proposed indication.

Eligible patients with primary metastatic NPC that was not suitable for local therapy at the time of the diagnosis or who had local-regional recurrence and/or distance metastasis were randomized in a 1:1 ratio to either:

- Arm A, penpulimab + gemcitabine + cisplatin/carboplatin every 3 weeks (Q3W) for up to 6 cycles, followed by penpulimab monotherapy Q3W or
- Arm B (control arm): placebo + gemcitabine + cisplatin/carboplatin, Q3W for up to 6 cycles, followed by placebo monotherapy Q3W. Penpulimab 200mg was administered as an intravenous infusion over 60 minutes Q3W.

Randomization was stratified by stage of disease (primary metastases vs. recurrent), ECOG (0 vs. 1), and liver metastasis (present vs. absent).

The primary efficacy endpoint to support approval was progression free survival (PFS) as assessed by Blinded Independent Committee Review (BICR) according to RECIST, version 1.1. The key secondary endpoint was overall survival (OS).

All patients must sign informed consent to up to 28 days before the first dose of study treatment. Baseline screening procedures, including physical exam, laboratory tests, ECG, echocardiogram, blood EBV-DNA, tumor imaging assessment, thyroid function test, CT or MRI of the brain, bone scan must be performed ≤ 28 days prior to initiation of treatment.

Tumor assessment with CT or MRI scan (chest/abdomen/pelvis) are to be performed at screening/baseline ≤ 28 days prior to initiation of treatment, approximately every 6 weeks within 54 weeks after the first dose and thereafter every 9 weeks until radiographic progression or discontinuation of study treatment (whichever occurs later), initiation of new anti-tumor therapy, loss to follow-up, death, withdrawal of consent, or study discontinued, whichever occurs first.

At the time of the data cut-off date (April 29, 2024), the study was ongoing. The study had enrolled 291 subjects (144 in the chemotherapy plus penpulimab arm, 147 in the chemotherapy plus placebo arm) across 36 study sites in China, seven sites in Brazil, two sites in US and one site in Canada.

III. RESULTS (by site)

1. **Dr. Feng Liu (Site # 1004)**
   No. 283, Tongzipo Road
   Yuelu District, Changsha
   Hunan, China

   Inspection dates: March 17 – 21, 2025

Dr. Liu was inspected as BIMO review-based inspection for Study AK105-304. This was the first inspection for this investigator.

At the time of the inspection, the site had screened 73 subjects, 54 of whom were enrolled in the AK105-304 study.

Source records for all 54 subjects enrolled at the site were reviewed. Records reviewed included, but were not limited to informed consent form, eligibility criteria and adverse event reporting. No significant discrepancies were found when source data were compared with the data submitted to the BLA.

The inspection also verified that radiology studies to assess the primary efficacy endpoint were performed according to protocol specified time points and all scans were submitted for central review.

Subject ID (b) (6) had a tumor assessment conducted at Week 56 of the study (b) (6) that was not submitted to for central review. The subject was randomized on (b) (6) to the control arm and received only one cycle of cisplatin and gemcitabine on C1D1 and C1D8). She experienced a serious event of cerebral infarction 12 days after the last dose of chemotherapy. Study treatment was interrupted and later discontinued per patient's request. The subject had two scans that were assessed by the BICR (Week 42, (b) (6) and Week 48, (b) (6)), both showing stable disease. The MRI scan performed on Week 56 (b) (6)) was assessed by the local radiologist as stable disease.

<u>Reviewer's comment:</u> it is noted that the data from Subject (b) (6) is included in the PFS assessment, censored on (b) (6) the date of the last scan assessed by central review. The impact of the missing scan dated (b) (6) on the primary efficacy endpoint of PFS is likely minimal, if any. OSI defers to the review division to consider the impact of Subject (b) (6) efficacy data on overall study outcome, and censor as appropriate.

Notwithstanding the lapse in submitting one radiographic scan for central review in one subject described above, based on the preliminary results provided by the FDA field investigator, data generated by Dr. Liu appear to be acceptable in support of the BLA.

2. Dr. Chuanben Chen (Site # 1007)
No. 420, Fuma Road
Jin An District, Fuzhou
Fujian, China

Inspection dates: February 17 – 21, 2025

Dr. Chen was inspected as BIMO review-based inspection for Study AK105-304. This was the first FDA inspection for this investigator.

At the time of the inspection, the site had screened 22 subjects and enrolled 17 subjects,

of these, none were on treatment at the time of the inspection.

Source records for all 17 enrolled subjects were reviewed and compared with the data listings submitted to the BLA. Records reviewed included, but were not limited to, informed consent forms, eligibility criteria, and adverse event reporting. All subjects met eligibility criteria. No significant discrepancies were observed.

The inspection verified that imaging scans to evaluate the primary efficacy endpoint were performed as specified in the protocol and all scans were submitted for central review, consistent with the data submitted to the BLA. No significant discrepancies were observed.

Based on the inspection, the data generated at Dr. Chen's site appear acceptable in support of the proposed indication in the BLA.

3. **Dr. Song Qu (Site # 1023)**
No. 71, Hedi Road
Qingxiu District, Nanning
Guangxi, China

Inspection dates: March 10 – 14, 2025

Dr. Qu was inspected as BIMO review-based inspection for Study AK105-304. This was the first FDA inspection for this investigator.

At the time of the inspection, the site had screened 21 subjects and enrolled 17 in the study, of these, 7 subjects had died due to disease progression, 5 were in follow-up phase 3 subjects completed study treatment per the protocol, and 2 subjects withdrew from study,

Source records for all 16 subjects enrolled at the site were reviewed and compared with the data listings submitted to the BLA. Records reviewed included, but were not limited to, informed consent forms, eligibility criteria, and adverse event reporting. All subjects met eligibility requirements. There was no significant underreporting of AEs.

The inspection verified that radiographic scans to evaluate the primary efficacy endpoint were performed as specified in the protocol and scans were submitted for central review, findings were consistent with the data submitted to the BLA.

Deficiencies in record keeping were noted during the inspection, however, they do not impact on patient safety or data reliability.

Based on the preliminary results provided by the FDA field investigator, the data generated at Dr. Qu' s site appear acceptable in support of the proposed indication in the BLA.

4. **Akeso Biopharma Co., Ltd**
   6 Shennong Road, Torch Development Zone
   Zhongshan, Guangdong
   China

   Inspection dates: March 3 – 7, 2025.

   This inspection assessed Akeso's oversight responsibilities for Study AK105-304. This was the first inspection for this Sponsor.

   Documents reviewed included monitoring process and reports, informed consent documents, written procedures, safety and adverse event management plan and reporting. Monitoring files for three clinical sites (Sites 1005, 1007, and 1029) were reviewed in depth for compliance. No issues were noted.

   The inspection did not observe issues related to safety/adverse event handling or reporting for AK105-304 study.

   Based on the preliminary results provided by the FDA field investigator, Akeso's overall oversight of the study and monitoring of the clinical investigators appear adequate.

5. (b) (4)

   Inspection dates: February 24 – 28, 2025.

   This inspection reviewed (b) (4) responsibilities to perform an independent central imaging review for Study AK105-304. This was the first FDA inspection for this imaging CRO.

   Records reviewed included, but were not limited to, (b) (4) procedures regarding the receipt, evaluation of radiographic images, blinding, adjudication procedures and transfer of data. The review found the processes adequate.

   The inspection verified response data for 24 subjects (12 in the chemotherapy plus placebo arm and 12 in chemotherapy plus penpulimab arm) enrolled in study AK105-304 were verified. Source data was compared to the efficacy line listing submitted to the BLA. No discrepancies were observed. The ID of these subjects are as follow:

Chemotherapy plus Placebo Arm		Chemotherapy plus Penpulimab Arm	
SUBJID	SITEID	SUBJID	SITEID
(b) (6)	1042	(b) (6)	1007
	1001		1004
	1001		1009
	1001		1018
	1002		1001
	1002		1001
	1002		1001
	1004		1002
	1004		1001
	1005		1001
	1007		1001
	1007		1001

Based on the preliminary results provided by the FDA field investigator, the imaging review data generated by (b) (4) appear acceptable in support of the proposed indication in the BLA.

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Lee Pai-Scherf, MD
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Division of Clinical Compliance Evaluation
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Review Division /Project Manager/Aisida Bamidele
OSI/DCCE/GCPAB/Program Analyst/Yolanda Patague

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/s/

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JENN W SELLERS
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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:	February 27, 2025
To:	Ashley Lane, MS Senior Regulatory Health Project Manager **Division of Oncology II (DO2)**
Through:	LaShawn Griffiths, MSHS-PH, BSN, RN Associate Director for Patient Labeling **Division of Medical Policy Programs (DMPP)** Barbara Fuller, RN, MSN, WOCN Team Leader, Patient Labeling **Division of Medical Policy Programs (DMPP)** Ruth Mayrosh, PharmD Senior Patient Labeling Reviewer **Division of Medical Policy Programs (DMPP)**
From:	Jessica Chung, PharmD, MS Patient Labeling Reviewer **Division of Medical Policy Programs (DMPP)** Roseline Boateng, PharmD, BCPS Regulatory Review Officer **Office of Prescription Drug Promotion (OPDP)**
Subject:	Review of Patient Labeling: Medication Guide (MG)
Drug Name (established name):	Penpulimab-kcqx
Dosage Form and Route:	injection, for intravenous use
Application Type/Number:	BLA 761258
Applicant:	Akeso Biopharma Co., Ltd. c/o Akesobio, Inc.

1 INTRODUCTION

On October 2, 2024, Akeso Biopharma Co., Ltd. c/o Akesobio, Inc. submitted for the Agency's review a Class 2 Resubmission of their original Biologics License Application (BLA) 761258 for penpulimab-kcqx injection, in response to the Agency Complete Response (CR) letter dated January 19, 2024. The proposed indications for penpulimab-kcqx injection are:

- in combination with gemcitabine and cisplatin or carboplatin as first-line treatment of patients with recurrent or metastatic nasopharyngeal carcinoma (NPC).
- for the treatment of metastatic non-keratinizing NPC with disease progression on or after platinum-based chemotherapy and at least one other prior line of therapy.

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 Oncology II (DO2) on October 30, 2024, for DMPP and OPDP to review the Applicant's proposed Medication Guide (MG) for penpulimab-kcqx injection.

2 MATERIAL REVIEWED

- Draft penpulimab-kcqx injection MG received on October 2, 2024, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on February 20, 2025.
- Draft penpulimab-kcqx injection Prescribing Information (PI) received on October 2, 2024, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on February 20, 2025.

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.

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.

In our collaborative review of the MG we:

- simplified wording and clarified concepts where possible
- ensured that the MG is consistent with the PI
- removed unnecessary or redundant information

- ensured that the MG is free of promotional language or suggested revisions to ensure that it is free of promotional language
- ensured that the MG meets the Regulations as specified in 21 CFR 208.20
- ensured that the MG meets the criteria as specified in FDA's Guidance for Useful Written Consumer Medication Information (published July 2006)

4 CONCLUSIONS

The MG is 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 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.

Please let us know if you have any questions.

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

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

Memorandum

Date: February 25, 2025

To: Ashley Lane, MS, Regulatory Project Manager, [Division of Oncology 2 (DO2)]

From: Roseline Boateng, PharmD, BCPS, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Emily Dvorsky, PharmD, RAC, Team Leader, OPDP

Subject: OPDP Labeling Comments for PENPULIMAB-KCQX injection, for intravenous use

BLA: 761258

Background:
In response to DO2's consult request dated October 30, 2024, OPDP has reviewed the proposed Prescribing Information (PI), Medication Guide, and carton and container labeling for the original BLA submission for Penpulimab-kcqx.

PI/Medication Guide:
OPDP's review of the proposed PI is based on the draft labeling emailed to OPDP on February 19, 2025, and our comments are provided below.

OPDP comments on the proposed Medication Guide will be sent under separate cover, either as a combined OPDP and Division of Medical Policy Programs (DMPP) review or a separate OPDP review.

Carton and Container Labeling:
OPDP's review of the proposed carton and container labeling is based on the draft labeling accessed from SharePoint on February 20, 2025, and we do not have any comment at this time.

Thank you for your consult. If you have any questions, please contact Roseline Boateng at 301-796-7506 or Roseline.Boateng@fda.hhs.gov.

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MEMORANDUM
REVIEW OF REVISED LABEL AND LABELING

Division of Medication Error Prevention and Analysis 2 (DMEPA 2)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

*** This document contains proprietary information that cannot be released to the public***

Date of This Review:	February 24, 2025
Requesting Office or Division:	Division of Oncology 2 (DO2)
Application Type and Number:	BLA 761258
Product Name, Dosage Form, and Strength:	Penpulimab-kcqx injection, 100 mg/10 mL (10 mg/mL)
Applicant Name:	Akeso Biopharma Co., Ltd
FDA Received Date:	February 20, 2025
TTT ID #:	2024-11223-2
DMEPA 2 Safety Evaluator:	Sali Mahmoud, PharmD, BCPS
DMEPA 2 Team Leader:	Tingting Gao, PharmD

1 PURPOSE OF MEMORANDUM

Akeso Biopharma Co., Ltd submitted revised carton labeling received on February 20, 2025 for Penpulimab-kcqx. The Division of Oncology 2 (DO2) requested that we review the revised carton labeling for Penpulimab-kcqx (Appendix A) to determine if it is 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

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

[a] Mahmoud, S. Review of Revised Label and Labeling for Penpulimab-kcqx (BLA 761258). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2025 FEB 12. TTT ID: 2024-11223-1.

APPENDIX A. IMAGES OF LABELS AND LABELING RECEIVED ON FEBRUARY 20, 2025

Carton Labeling:

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/s/

SALI MAHMOUD
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MEMORANDUM
REVIEW OF REVISED LABEL AND LABELING

Division of Medication Error Prevention and Analysis 2 (DMEPA 2)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

*** This document contains proprietary information that cannot be released to the public***

Date of This Review:	February 12, 2025
Requesting Office or Division:	Division of Oncology 2 (DO2)
Application Type and Number:	BLA 761258
Product Name, Dosage Form, and Strength:	Penpulimab-kcqx injection, 100 mg/10 mL (10 mg/mL)
Applicant Name:	Akeso Biopharma Co., Ltd
FDA Received Date:	February 10, 2025
TTT ID #:	2024-11223-1
DMEPA 2 Safety Evaluator:	Sali Mahmoud, PharmD, BCPS
DMEPA 2 Team Leader:	Tingting Gao, PharmD

1 PURPOSE OF MEMORANDUM

Akeso Biopharma Co., Ltd submitted revised container label and carton labeling received on February 10, 2025 for Penpulimab-kcqx. The Division of Oncology 2 (DO2) requested that we review the revised container label and carton labeling for Penpulimab-kcqx (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

The revised container label is acceptable from a medication error perspective. However, the carton labeling is unacceptable from a medication error perspective. The phrase "Medication Guide to each patient" is incorrectly repeated on the principal display panel of the carton labeling.

3 RECOMMENDATIONS FOR AKESO BIOPHARMA CO., LTD

A. Carton Labeling

1. On the principal display panel, we recommend deleting (b) (4) (b) (4) to reduce redundancy.
2. On the principal display panel, we recommend adding more white space between the route of administration statement and the ATTENTION PHARMACIST statement to improve readability.
3. Revise the statement "Single-dose vial.Discard unused portion." to include a space between the sentences. For example, "Single-dose vial. Discard unused portion."
4. On the side panel, consider revising the word "Prescrib- ing" so that the entire word "Prescribing" appears on one line for clarity.

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

[a] Mahmoud, S. Label and Labeling Review for Penpulimab-kcqx (BLA 761258). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2025 JAN 14. TTT ID: 2024-11223.

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LABEL AND LABELING REVIEW

Division of Medication Error Prevention and Analysis 2 (DMEPA 2)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

*** This document contains proprietary information that cannot be released to the public***

Date of This Review:	January 14, 2025
Requesting Office or Division:	Division of Oncology 2 (DO2)
Application Type and Number:	BLA 761258
Product Name, Dosage Form, and Strength:	Penpulimab-kcqx Injection, 100 mg/10 mL (10 mg/mL)
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant Name:	Akeso Biopharma Co., Ltd
FDA Received Date:	October 2, 2024; October 8, 2024
TTT ID #:	2024-11223
DMEPA 2 Safety Evaluator:	Sali Mahmoud, PharmD, BCPS
DMEPA 2 Team Leader:	Tingting Gao, PharmD

1 INTRODUCTION

As part of the approval process for Penpulimab-kcqx Injection, the Division of Oncology 2 (DO2) requested that we review the proposed Penpulimab-kcqx Prescribing Information (PI), Medication Guide (MG), container label(s), and carton labeling for areas of vulnerability that may lead to medication errors.

1.1 REGULATORY HISTORY

Akeso Biopharma Co., Ltd previously submitted BLA 761258 on June 11, 2021, which received a Complete Response letter on January 19, 2024 due to clinical and product quality deficiencies.[a]

Thus, Akeso Biopharma Co., Ltd submitted a Class 2 Resubmission on October 2, 2024.[b]

2 MATERIALS CONSIDERED

This section lists the materials considered for our review of BLA 761258.

Table 1. Materials Considered for this Review	
Materials Considered	Appendix Section
Relevant Product Information	A
Labels and Labeling	B
Previous DMEPA Reviews	C

3 CONCLUSION

The proposed Penpulimab-kcqx Medication Guide (MG) is acceptable from a medication error perspective.

However, the proposed Prescribing Information (PI), container label(s), and carton labeling may be improved to promote safe use of this product from a medication error perspective. We provide the identified medication error issues, our rationale for concern, and our proposed recommendations to minimize the risk for medication error for the Division of Oncology 2 (DO2) in Section 4 and for Akeso Biopharma Co., Ltd in Section 5.

[a] Lane, Ashley on behalf of Paul Kluetz. Complete Response for BLA 761258. Silver Spring (MD): FDA, CDER, OND, Division of Oncology 2 (DO2) (US); 2024 JAN 19.
[b] Class 2 Resubmission for Penpulimab-kcqx (BLA 761258). Zhongshan (China): Akeso Biopharma Co., Ltd; 2024 OCT 02. Available from: \\CDSESUB1\EVSPROD\bla761258\0078\m1\us\12-cover-letter\cover-letter-ak105-bla-761258-0078-20240930-clean.pdf.

4 RECOMMENDATIONS FOR THE DIVISION OF ONCOLOGY 2 (DO2)

A. Prescribing Information

1. Section 2 Dosage and Administration

a. In Section 2.1 Recommended Dosage, consider deleting (b) (4) (b) (4) to minimize confusion.

b. In Section (b) (4) Preparation and Administration, the preparation instructions do not direct user to protect the diluted solution from light. Clarify if the diluted solution should be protected from light.

c. In Section (b) (4) Preparation and Administration, consider revising the preparation instructions to only use one subset of bulletins instead of two subsets of bulletins to minimize confusion. For example:

d. In Section (b) (4) Preparation and Administration, as currently presented, the term "diluted solution" and (b) (4) are being used interchangeably. Consider select one term (e.g., "diluted solution") and use it consistently throughout the Storage of Diluted Solution subsection.

2. Section 16 How Supplied/Storage and Handling

a. We recommend removing (b) (4) (b) (4) since this information is not needed in Section 16.

5 RECOMMENDATIONS FOR AKESO BIOPHARMA CO., LTD

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

1. As currently presented, the graphic (e.g., multiple horizontal lines and the upside down V) on the bottom of the principal display panel (PDP) competes with the prominence of the critical information on the PDP. The proprietary name and established or proper name along with the product strength, route of

administration, and warnings or cautionary statements should be the most prominent information on the principal display panel (PDP). We recommend decreasing the prominence of your graphic relative to the prominence of the critical information on the PDP needed for proper identification and use of your proposed product in accordance with 21 CFR 201.15(a)(6). For example, this may be accomplished through increasing the prominence of the critical information statements and minimizing the size of the graphic.

2. The strength statement "100mg/10 mL" does not contain a space between 100 and mg. Ensure that there is a space between "100" and "mg" for readability so that the statement reads "100 mg/10 mL".

3. The storage statement is inconsistent with the storage information in the prescribing information: (b) (4) (b) (4) Revise the storage statements to "Store refrigerated at 2°C to 8°C (36°F to 46°F) in the original carton to protect from light. Do not shake. Do not freeze." for consistency with the prescribing information.

4. On the side panel, revise the dosage statement to state "Recommended Dosage: See Prescribing Information" to be consistent with the recommended dosage information in the Prescribing Information.

B. Container Label(s)

1. The instructions for pharmacist to dispense medication guide are (b) (4) (b) (4) which may be overlooked. We recommend relocating the "ATTENTION PHARMACIST" message from the side panel to the PDP in accordance with 21 CFR 208.24(d). We recommend revising this statement to "ATTENTION PHARMACIST: Dispense the enclosed Medication Guide to each patient." to use active voice instead of passive voice.

2. On the PDP, we recommend increasing the font size of the smaller text (e.g., text that are presented in Arial 3.2 pt) to increase readability of critical information such as the route of administration, the "ATTENTION PHARMACIST" statement, and the package type term. Ensure there is sufficient white space between each paragraph to improve readability and to reduce clutter.

C. Carton Labeling

1. On the PDP, we recommend increasing the font size of the smaller text (e.g., text that are presented in Arial 6.5 pt) to a minimum of font size of Arial 10 pt to increase readability of critical information such as the route of administration, the "ATTENTION PHARMACIST" statement, and the package type term. Ensure there is sufficient white space between each paragraph to improve readability and to reduce clutter.

2. We recommend revising the "ATTENTION PHARMACIST" statement to "ATTENTION PHARMACIST: Dispense the enclosed Medication Guide to each patient." (b) (4)
3. To increase the prominence of the "ATTENTION PHARMACIST" statement, we recommend relocating the package type term "Single-dose vial. Discard unused portion." to the bottom of the PDP. Additionally, we recommend the addition of more white space between the route of administration statement and the "ATTENTION PHARMACIST" statement. For example:

   For intravenous infusion after dilution

   Attention pharmacist: Dispense the enclosed Medication Guide to each patient.

   Single-dose vial. Discard unused portion.

4. On the side panel, delete (b) (4) to reduce clutter.
5. On one or two of the side panels, consider deleting (b) (4) to allow sufficient space to increase the font size of the smaller text (e.g., text that are presented in Arial 5 pt) to a minimum of font size of Arial 10 pt to increase readability of these information. Ensure there is sufficient white space between each paragraph to improve readability and to reduce clutter.
6. Add to side panel of the carton "Infuse immediately after dilution. If immediate use is not possible, store the diluted solution up to 4 hours either at room temperature 20°C to 25°C (68°F to 77°F), or refrigerated at 2°C to 8°C (36°F to 46°F). Discard after 4 hours."

APPENDICES: MATERIALS CONSIDERED FOR THIS REVIEW

APPENDIX A. RELEVANT PRODUCT INFORMATION

Table 2 presents relevant product information for penpulimab-kcqx received on October 8, 2024 from Akeso Biopharma Co., Ltd.

Table 2. Relevant Product Information for Penpulimab-kcqx	
Initial Approval Date	N/A
Nonproprietary Name	penpulimab-kcqx
Indication	First line treatment of recurrent or metastatic nasopharyngeal carcinoma (NPC) in combination with gemcitabine and cisplatin or carboplatin. Metastatic non-keratinizing NPC with disease progression on or after platinum-based chemotherapy and at least one other prior line of therapy.
Dosage Form	Injection
Strength	100 mg/10 mL (10 mg/mL)
Route of Administration	Intravenous
Dose and Frequency	First-line Treatment of Recurrent or Metastatic NPC 200 mg intravenous infusion over 60 minutes every 3 weeks. Continue treatment until disease progression or unacceptable toxicity, for a maximum of 24 months. Recurrent Metastatic Non-Keratinizing NPC 200 mg intravenous infusion over 60 minutes every 2 weeks . Continue treatment until disease progression or unacceptable toxicity, for a maximum of 24 months.
How Supplied	Carton containing one 100 mg/10 mL (10 mg/mL) single-dose vial
Storage	Store refrigerated at 2°C to 8°C (36°F to 46°F) in the original carton to protect from light. Do not shake. Do not freeze.
Container Closure	10 mL (b) (4) glass vial with rubber stopper and an aluminum cap with a plastic flip-off disk

APPENDIX B. LABELS AND LABELING

B.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 Penpulimab-kcqx labels and labeling submitted by Akeso Biopharma Co., Ltd.

- Prescribing Information received on October 8, 2024, available from \\CDSESUB1\EVSPROD\bla761258\0080\m1\us\114-labeling\114a-draft-label\draft-uspi-penpulimab-bla761258-20241008-tracked.docx
- Medication Guide received on October 8, 2024, available from \\CDSESUB1\EVSPROD\bla761258\0080\m1\us\114-labeling\114a-draft-label\draftmedguide-penpulimab-bla761258-20241008-tracked.docx
- Container label(s) received on October 2, 2024
- Carton labeling received on October 2, 2024

B.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.

APPENDIX C. PREVIOUS DMEPA REVIEWS

On January 7, 2025, we searched for previous DMEPA reviews relevant to this current review using the terms, penpulimab. Our search identified 3 previous review(s)[d,e,f], and we considered our previous recommendations to see if they are applicable for this current review.

[d] Mahmoud, S. Label and Labeling Review for Penpulimab-kcqx (BLA 761258). Silver Spring (MD): FDA, CDER, OSE, DMEPA2 (US); 2021 DEC 22. RCM No.: 2021-1085.

[e] Mahmoud, S. Review of Revised Label and Labeling for Penpulimab-kcqx (BLA 761258). Silver Spring (MD): FDA, CDER, OSE, DMEPA2 (US); 2022 JUN 28. RCM No.: 2021-1085-1.

[f] Mahmoud, S. Review of Revised Label and Labeling for Penpulimab-kcqx (BLA 761258). Silver Spring (MD): FDA, CDER, OSE, DMEPA2 (US); 2022 JUL 21. RCM No.: 2021-1085-2.

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Addendum Clinical Inspection Summary

Date	December 14, 2023
From	Lee Pai-Scherf, MD Michele Fedowitz, MD, Team Leader Jenn Sellers, MD, PhD, Branch Chief Good Clinical Practice Assessment Branch (GCPAB) Division of Clinical Compliance Evaluation (DCCE) Office of Scientific Investigations (OSI)
To	Satinder Choudhary, Clinical Reviewer Nicole Drezner, MD, Deputy Division Director Division of Oncology 2/Office of Oncologic Products
BLA #	761258
Applicant	Akeso Biopharma Co., Ltd.
Drug	Penpulimab
NME (Yes/No)	Yes
Therapeutic Classification	Monoclonal Antibody
Proposed Indication(s)	Nasopharyngeal cancer (NPC)
Consultation Request Date	09/10/2021
Summary Goal Date	06/03/2022
CIS Filed in DARRTS	05/31/2022
Action Goal Date	07/14/2022
PDUFA Date	07/15/2022 (initial), 10/16/2022 (extended due to major amendment). Action deferred due to inability to inspect manufacturing sites in China due to COVID-19 pandemic

I. OVERALL ASSESSMENT OF FINDINGS AND RECOMMENDATIONS

Clinical data from Study AK105-202, solely conducted in China, were submitted by Akeso Biopharma Co., Ltd on July 23, 2021, in support of this Biologics License Application (BLA) for penpulimab for the treatment of nasopharyngeal cancer (NPC). Three clinical investigators (CI), Drs. Jingao Li (Site # 03), Qingfeng Zou (Site # 04), Xiaozhong Chen (Site # 05), as well as the Sponsor, Akeso Biopharma, and the imaging contract research organization (CRO), (b) (4), were selected for inspection.

The inspection of the imaging CRO, (b) (4) was conducted in November 2021, which did not reveal any significant findings. Please refer to the Clinical Inspection Summary (CIS) dated May 31, 2022, for details.

The inspections of CIs, Drs. Li, Zou, and Chen were significantly delayed due to travel restrictions in China related to COVID-19 pandemic. These inspections were recently completed and did not reveal any data discrepancies or significant regulatory violations. Based on the results of these inspections, Study AK105-202 appears to have been conducted

adequately and the data generated by the inspected sites appear acceptable in support of the proposed indications in the BLA.

Of note, the inspection result of Dr. Li (Site # 03) is based on a summary provided by the field inspector and is therefore preliminary. If significant information is contained in the final Establishment Inspection Report (EIR), an addendum to this clinical inspection summary will be filed.

Inspection of the Sponsor, Akeso Biopharma, was cancelled at the request of the division per email communication dated November 2, 2023, and December 5, 2023.

II. BACKGROUND

Akeso Biopharma Co., Ltd submitted BLA 761258 seeking approval for penpulimab for the treatment of patients with metastatic nonkeratinizing NPC with disease progression on or after platinum-based chemotherapy and at least one other prior line of therapy.

Data from a non-US IND study, AK105-202, was submitted to support the BLA. AK105-202 enrolled a total of 130 subjects across 20 clinical sites in China.

The primary endpoint of the study was overall response rate (ORR) per RECIST v1.1 as assessed by an independent central imaging assessment (BICR). The key secondary endpoints were the duration of response (DoR), progression-free survival (PFS), overall survival (OS) and to assess the pharmacokinetics, immunogenicity, and safety.

At the time of the submission, DO2 requested inspections of 3 CIs, Drs. Jingao Li (Site # 03), Qingfeng Zou (Site # 04), and Xiaozhong Chen (Site # 05). Due to ongoing travel restrictions related to COVID-19 pandemic at the time, OSI was not able to conduct the on-site CI inspections in China until recently. This CIS addendum summarizes the inspection results for these 3 CIs.

III. RESULTS

1. **Dr Jingao Li (Site # 03)**
   519 Beijing East Road
   Quingshanhu District, Nanchang City
   Nanchang, Jiangxi 330029
   CHINA

   Inspection dates: November 6 – November 10, 2023

   The official establishment inspection report (EIR) is pending. The review below is from the summary close out email and communication with the inspector during the

inspection. This report will be updated after review of the official EIR, if relevant additional significant information is included.

Dr. Li was inspected as a routine PDUFA inspection for Study AK105-202. This was the first FDA inspection of this investigator.

At the time of the inspection, the site enrolled 13 subjects in the study, of which, 2 subjects were in follow-up phase, 2 withdrew from study due to disease progression, one subject was lost to follow-up and 8 subjects had died due to disease progression.

Source records for 6 subjects were reviewed in full. Records reviewed included informed consent documents, eligibility criteria, study assessment for each visit date, protocol deviations, AE and SAE reports, investigational drug administration information and tumor assessment imaging documents. No regulatory violations or data discrepancies were observed.

Based on the results of the inspection, the study was conducted in accordance with the investigational plan and the data generated at Dr. Li's site appear acceptable in support of the proposed indication in the BLA.

2. Dr. Qingfeng Zou (Site # 04)
78 Hengzhigang
Yuexiu District, Guangzhou City
Guangdong Province 528400
CHINA

Inspection dates: September 5 – September 8, 2023

Dr. Zou was inspected as a routine PDUFA inspection for Study AK105-202. This was the first FDA inspection of this investigator.

At the time of the inspection, the site had screened 18 subjects and enrolled 15 subjects in the study: 2 subjects remain on active treatment, 4 subjects completed study treatment, 3 withdrew consent, 5 subjects withdrew from study due to disease progression, and one subject had died.

Source records for all 15 enrolled subjects and 1 screen failure were reviewed and compared with the data submitted to the BLA. Records reviewed included informed consent documents, eligibility criteria, AE and SAE reports, protocol deviations, tumor assessment imaging documents, and investigational drug administration records. There was no evidence of under-reporting of AEs or unreported protocol violations.

Additional records reviewed during the inspection included, but were not limited to, drug accountability, staff qualifications, financial disclosure forms, Ethic Committee approvals, delegation of authority logs, and monitoring reports. No issues were

identified.

Based on the results of the inspection, the study was conducted in accordance with the investigational plan and the AK105-202 study data generated at Dr. Zou's site appear acceptable in support of the proposed indication in the BLA.

3. **Dr. Xiaozhong Chen (Site # 05)**
1 Banshan East Road
Gongshu District, Hangzhou 310022
CHINA

Inspection dates: September 11 – September 15, 2023

Dr. Chen was inspected as a routine PDUFA inspection for Study AK105-202. This was the first FDA inspection of this investigator.

At the time of the inspection, the site had screened 24 subjects and enrolled 21 subjects in the study. Two subjects remained on active treatment and 19 subjects had completed the study.

Source records for all 21 subjects enrolled at the site were reviewed and compared with study data. The inspection covered informed consent procedures, subjects meeting the inclusion/exclusion criteria, overall protocol integrity and compliance, serious adverse event reporting, and protocol deviations. No discrepancies were observed. There was no evidence of under-reporting of AEs or SAEs or protocol deviations. Tumor imaging assessments were performed according to the protocol and were submitted for Sponsor/Imaging CRO for central review.

Additional records reviewed include, but were not limited to, Ethic Committee approvals, drug accountability, facility adequacy, staff training and qualifications. correspondence between site and sponsor and monitoring reports.

Based on the results of the inspection, the data generated at Dr. Chen's site appear acceptable in support of the proposed indication in the BLA.

{See appended electronic signature page}

Lee Pai-Scherf, MD
Good Clinical Practice Assessment Branch
Division of Clinical Compliance Evaluation
Office of Scientific Investigations

CONCURRENCE:

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Michele Fedowitz, MD
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CONCURRENCE: {*See appended electronic signature page}*

Jenn Sellers, MD, PhD
Branch Chief
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CC:

DARRTS: BLA 761258
Review Division /Project Manager/Ashley Lane
OSI/DCCE/GCPAB/Program Analyst/Yolanda

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Labeling Review

Application Type	BLA
Application Number(s)	761258
Priority or Standard	Standard
Submit Date(s)	July 16, 2021
Received Date(s)	July 16, 2021
PDUFA Goal Date	October 16, 2022
Division/Office	Division of Oncology 2
Established Name	Penpulimab-kcqx
(Proposed) Trade Name	(b) (4)
Pharmacologic Class	Programmed death receptor-1 (PD-1) blocking antibody
Applicant	Akeso Biopharma Co., Ltd.
Formulation(s)	10 mg/mL, 10 mL
Dosing Regimen	Injection for IV infusion
Applicant Proposed Indication(s)/Population(s)	Nasopharyngeal carcinoma
Recommendation on Regulatory Action	Complete Response
Recommended Indication(s)/Population(s) (if applicable)	For the treatment of adult (b) (4) with metastatic non-keratinizing nasopharyngeal carcinoma with disease progression on or after platinum-based chemotherapy and at least one other prior line of therapy.
Associate Director for Labeling	Barb Scepura, MSN, CRNP

Brief Background

Penpulimab is a monoclonal antibody targeting programmed death-1 (PD-1), an immune checkpoint inhibitor with an established pharmacological class of PD-1 blocking antibody indicated for the treatment of adult (b) (4) with metastatic non-keratinizing nasopharyngeal carcinoma with disease progression on or after platinum-based chemotherapy and at least one other prior line of therapy. For further details, please see the Assessment Aid review.

The October 2023 approval of LOQTORZI (toripalimab-tpzi) in combination with cisplatin and gemcitabine, for first-line treatment of adults with metastatic or with recurrent, locally advanced nasopharyngeal carcinoma (NPC); and as a single agent, for the treatment of adults with recurrent unresectable or metastatic NPC with disease progression on or after a platinum-containing chemotherapy, provides improved treatment options for these patients.

Because LOQTORZI offers superior treatment options for these patients, penpulimab-kcqx no longer meets the regulatory requirements for approval.

Due to the complete response action, final agreement on labeling was not reached during this review cycle. The table below contains brief descriptions of FDA proposed revisions and tracked, draft labeling is attached as a PDF for reference only.

FDA: Key Labeling Revisions

Label Section	Applicant Proposal	FDA Revision
1 INDICATIONS AND USAGE	(b) (4)	Indication revised to specify "recurrent metastatic non-keratinizing" nasopharyngeal carcinoma.
2 DOSAGE AND ADMINISTRATION		Specified the treatment duration "(b) (4) a maximum of 24 months." Inclusion of instructions for storage of diluted solution: Discard after 4 hours (b) (4)
5 WARNINGS AND PRECAUTIONS		Applicant proposed text was similar to other harmonized anti-PDL1 labeling. Revisions for clarity and specificity to this product made throughout.
6 ADVERSE REACTIONS		FDA included the most common adverse reactions and Grade 3 or 4 laboratory abnormalities for the pooled population. Proposed text was extensively revised to include description of study eligibility, treatment received, actual exposure data, information on fatalities due to adverse reactions and dosage interruptions for adverse reactions. The proposed laboratory abnormalities table was replaced to include *All Grade* and Grade 3 or 4.

		(b) (4) [redacted]
8 USE IN SPECIFIC POPULATIONS	Application specific text supporting pregnancy, lactation, pediatric use, and geriatric use.	Pregnancy, Lactation and Females and Males of Reproductive Potential sections text revised for consistency with current labeling practices. (b) (4) [redacted] Geriatric section revised section in accordance with 21 CFR 201.57(c)(9)(v)(A).
11 DESCRIPTION	Application specific product description.	Minor revisions for consistency with current labeling practices.
12 CLINICAL PHARMACOLOGY	Application specific product description.	Major revisions to remove unnecessary speculative and potentially promotional text. Subsection 12.2 Pharmacodynamics section added to comply with the 21 CFR 201.57(c)(13)(i)(B) requirements. Subsection 12.3 Extensive revisions to remove unnecessary text and clarify the data. (b) (4) [redacted]
13 NONCLINICAL TOXICOLOGY	Application specific product description.	Text revised for consistency with current labeling practices. Inclusion of information from 2021 study by Kauffman et al. in which investigators evaluated the role of PD-1 during Mycobacterium tuberculosis infection of rhesus macaques. PD-1 blockade using a primate anti-PD1 antibody was also shown to exacerbate M.

		tuberculosis infection in rhesus macaques. PD-1 and PD-L1 knockout mice have also shown decreased survival following infection with lymphocytic choriomeningitis virus.
14 CLINICAL STUDIES	Application specific product description.	Revised to include prognostic (data description of previously received treatments and percentage of patients enrolled by TPS scores (<1%, 1-49%, ≥ 50%)
16 HOW SUPPLIED/STORAGE AND HANDLING		Minor revisions for clarity.
17 PATIENT COUNSELING	Proposed text consistent with other anti-PDL1 labeling.	Minor revisions for clarity.

Draft tracked labeling, March 2022

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MEMORANDUM

REVIEW OF REVISED LABEL AND LABELING
Division of Medication Error Prevention and Analysis 2 (DMEPA 2)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

Date of This Memorandum:	July 21, 2022
Requesting Office or Division:	Division of Oncology 2 (DO2)
Application Type and Number:	BLA 761258
Product Name and Strength:	penpulimab-kcqx injection, 100 mg/10 mL (10 mg/mL)
Applicant/Sponsor Name:	Akeso Biopharma Co., Ltd
OSE RCM #:	2021-1085-2
DMEPA 2 Safety Evaluator:	Sali Mahmoud, PharmD, BCPS
DMEPA 2 Team Leader:	Ashleigh Lowery, PharmD, BCCCP

1 PURPOSE OF MEMORANDUM

The Applicant submitted revised container label and carton labeling received on July 5, 2022 for penpulimab-kcqx. Division of Oncology 2 (DO2) requested that we review the revised container label and carton labeling for penpulimab-kcqx (Appendix A) to determine if it is 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

The revised container label and carton labeling is acceptable from a medication error perspective. We have no further recommendations.

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

[a] Mahmoud, S. Label and Labeling Review for penpulimab-kcqx (BLA 761258). Silver Spring (MD): FDA, CDER, OSE, DMEPA2 (US); 2022 JUN 28. RCM No.: 2021-1085-1.

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MEMORANDUM

REVIEW OF REVISED LABEL AND LABELING
Division of Medication Error Prevention and Analysis 2 (DMEPA 2)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

Date of This Memorandum:	June 27, 2022
Requesting Office or Division:	Division of Oncology 2 (DO2)
Application Type and Number:	BLA 761258
Product Name and Strength:	penpulimab-kcqx injection, 100 mg/10 mL (10 mg/mL)
Applicant/Sponsor Name:	Akeso Biopharma Co., Ltd
OSE RCM #:	2021-1085-1
DMEPA 2 Safety Evaluator:	Sali Mahmoud, PharmD, BCPS
DMEPA 2 Team Leader:	Ashleigh Lowery, PharmD

1 PURPOSE OF MEMORANDUM

The Applicant submitted revised container label and carton labeling received on May 24, 2022 for penpulimab-kcqx. Division of Oncology 2 (DO2) requested that we review the revised container label and carton labeling for penpulimab-kcqx (Appendix A) to determine if it is 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

The revised container and carton labeling is unacceptable from a medication error perspective and can be improved for clarity. We provide recommendations in Section 3 below.

3 RECOMMENDATIONS FOR AKESO

We recommend the following be implemented prior to approval of this BLA:

A. General Comments (Container label and Carton Labeling)
   1. To better explain to whom this statement applies, change [(b) (4)] [(b) (4)] to "Attention Pharmacist: Dispense the enclosed Medication Guide to each patient."

[a] Mahmoud, S. Label and Labeling Review for penpulimab-kcqx (BLA 761258). Silver Spring (MD): FDA, CDER, OSE, DMEPA2 (US); 2021 DEC 20. RCM No.: 2021-1085.

2. To improve prominence, bold the statement “Must be Refrigerated.”

B. Container label

1. Add the product’s linear barcode to each individual container as required per 21CFR 201.25(c)(2). Ensure that the linear barcode in a vertical position to improve the scannability of the barcode. Barcodes placed in a horizontal position may not scan due to vial curvature.

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Clinical Inspection Summary

Date	May 31, 2022
From	Lee Pai-Scherf, MD Karen Bleich, MD (TL) Kassa Ayalew, MD, MPH Good Clinical Practice Assessment Branch (GCPAB) Division of Clinical Compliance Evaluation (DCCE) Office of Scientific Investigations (OSI)
To	Erica Nakajima MD/Satinder Choudary (Clinical Reviewers) Nicole Drezner, MD, Team Leader Martha Donoghue, MD, Deputy Division Director Division of Oncology 2/ Office of Oncologic Products
BLA #	761258
Applicant	Akeso Biopharma Co., Ltd.
Drug	Penpulimab
NME (Yes/No)	Yes
Therapeutic Classification	Monoclonal Antibody
Proposed Indication(s)	Nasopharyngeal cancer (NPC)
Consultation Request Date	09/10/2021
Summary Goal Date	06/03/2022
Action Goal Date	07/14/2022
PDUFA Date	07/15/2022

I. OVERALL ASSESSMENT OF FINDINGS AND RECOMMENDATIONS

Clinical data from Study AK105-202, primarily conducted in China, were submitted in support of this Biologic Drug Application (BLA) for penpulimab. Three clinical investigators, Drs. Jingao Li (Site # 03), Dr. Qingfeng Zout (Site # 04), Xiaozhong Chen (Site # 05), the Sponsor, Akeso Biopharma, and the imaging CRO, (b) (4), were selected for clinical inspection.

Inspection of the selected clinical investigators and the Sponsor have been delayed due to ongoing travel restrictions related to the COVID-19 pandemic in China.

On-site inspection revealed no significant findings at the imaging CRO (b) (4) site. Based on the result of the inspection, data generated by the imaging CRO appears acceptable in support of the proposed indication in the BLA.

II. BACKGROUND

Penpulimab injection (AK105) is a human IgG1 monoclonal antibody that binds to PD-1 and blocks the interaction of PD-1 with PD-L1 and PD-L2. Akeso Biopharma Co., Ltd submitted BLA 761258 seeking approval for penpulimab for the treatment of patients with metastatic nonkeratinizing NPC with disease progression on or after platinum-based chemotherapy and at least one other prior line of therapy.

This is the first marketing application submitted by Akeso to the US. Data from a non-US IND study, AK105-202, was submitted to support the BLA. AK105-202 enrolled a total of 130 subjects across 20 clinical sites in China.

The primary objective is to estimate the anti-tumor activity in terms of overall response rate (ORR) assessed by an independent central imaging assessment (IRCC) per RECIST v1.1. The key secondary endpoints are duration of response (DoR), progression-free survival (PFS), overall survival (OS) and to assess the pharmacokinetics, immunogenicity and safety.

Tumor assessment and radiological imaging are performed at baseline and at pre-specified time points. All radiographic images are to be submitted to (b) (4), the central imaging facility responsible for central review of images, for independent assessment.

Three clinical investigators were identified for inspection: Jingao Li (Site # 03), Dr. Qingfeng Zout (Site # 04), Xiaozhong Chen (Site # 05) were selected primarily based on number of subjects enrolled and treatment effect. Akeso Biopharma was chosen for inspection given that this is the first marketing application submitted by this Sponsor. (b) (4) was chosen for evaluation of the conduct of the central imaging review and for evaluation of the primary efficacy endpoint.

III. RESULTS

(b) (4)

Inspection Dates: (b) (4)

(b) (4) was inspected as data audit and surveillance inspection for Study AK105-202. This CRO has been previously inspected on (b) (4) and (b) (4), resulting in NAI classifications.

The current inspection included the review of the following records: (b) (4) organizational charts, standard operating procedures, site personnel selection and training, software feature and access permissions, reports and audit trails, and communication plans.

Other records reviewed include study protocol and amendments, imaging charters, and electronic case report form (eCRF) extracts.

For Study AK105-202, radiographic images performed by the study sites are submitted to (b) (4) using the electronic transfer service and are automatically de-identified of any Protected Patient Health Information (PHI). Following receipt of the data, (b) (4) staff performed a quality control (QC) assessment according to the Imaging Collection and Handling plan. Once the QC process is completed, the images are submitted for blinded independent review. Imaging read results are stored in the company's (b) (4) (b) (4) database, made available for review via one report per subject and extracted for data transfer to the Sponsor.

The blinded independent reviewers were trained in the study protocol and thus not blinded to treatment in this single arm study. Per the imaging charter, the reviewers were blinded to subject demographics, site response assessments, and clinical information.

Two independent readers were randomly designated to each imaging study and blinded to each other's assessment. If both assessments did not yield the same assessment response, an adjudicator, blinded to the previous reads, was assigned to read the images, and determine the final assessment.

To verify the submitted imaging data, imaging reads from all 33 subjects reported to have a achieved a complete or partial response were reviewed against the data line listings for overall target lesion diameter, target lesion, new lesion, and overall response. No discrepancies were observed.

(b) (4) followed all procedures for contracted study related activities. The inspection found no regulatory violations at the site.

{See appended electronic signature page}

Lee Pai-Scherf, MD
Good Clinical Practice Assessment Branch
Division of Clinical Compliance Evaluation
Office of Scientific Investigations

CONCURRENCE:

{See appended electronic signature page}

Karen Bleich, MD
Team Leader,
Good Clinical Practice Assessment Branch
Division of Clinical Compliance Evaluation
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CONCURRENCE: {*See appended electronic signature page}*

Kassa Ayalew, MD, M.P.H
Acting Branch Chief
Good Clinical Practice Assessment Branch
Division of Clinical Compliance Evaluation
Office of Scientific Investigations

CC:

DARRTS: BLA 761258
Review Division /Project Manager/Ashley Lane
OSI/Database PM/Dana Walters
OSI/DCCE/GCPAB/Program Analyst/Yolanda

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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:	March 14, 2022
To:	Ashley Lane, MS Consumer Safety Officer **Division of Oncology 2 (DO2)**
Through:	LaShawn Griffiths, MSHS-PH, BSN, RN Associate Director for Patient Labeling **Division of Medical Policy Programs (DMPP)** Barbara Fuller, RN, MSN, CWOCN Team Leader, Patient Labeling **Division of Medical Policy Programs (DMPP)**
From:	Sharon R. Mills, BSN, RN, CCRP Senior Patient Labeling Reviewer **Division of Medical Policy Programs (DMPP)** Lynn Panholzer, PharmD Regulatory Review Officer **Office of Prescription Drug Promotion (OPDP)**
Subject:	Review of Patient Labeling: Medication Guide (MG)
Drug Name (established name):	(b) (4) (penpulimab-kcqx)
Dosage Form and Route:	injection, for intravenous use
Application Type/Number:	BLA 761258
Applicant:	Akeso Biopharma Co., Ltd. c/o Akesobio, Inc.

1 INTRODUCTION

On July 16, 2021, Akeso Biopharma Co., Ltd. c/o Akesobio, Inc. submitted for the Agency's review an original Biologics License Application (BLA) 761258 for [redacted](penpulimab-kcqx) injection. The proposed indication for [redacted] (penpulimab-kcqx) injection is for the treatment of adult [redacted] with metastatic non-keratinizing nasopharyngeal carcinoma with disease progression on or after platinum-based chemotherapy and at least one other prior line of therapy.

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 Oncology 2 (DO2) on July 21, 2021, for DMPP and OPDP to review the Applicant's proposed Medication Guide (MG) for [redacted] (penpulimab-kcqx) injection.

2 MATERIAL REVIEWED

- Draft [redacted](penpulimab-kcqx) injection MG received on July 16, 2021, and received by DMPP and OPDP on March 3, 2022.
- Draft [redacted](penpulimab-kcqx) injection Prescribing Information (PI) received on July 16, 2021, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on March 3, 2022.
- Approved KEYTRUDA (pembrolizumab) [BLA 125554] comparator labeling dated February 4, 2022.

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.

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.

In our collaborative review of the MG we:

- simplified wording and clarified concepts where possible
- ensured that the MG is consistent with the Prescribing Information (PI)

- removed unnecessary or redundant information
- ensured that the MG is free of promotional language or suggested revisions to ensure that it is free of promotional language
- ensured that the MG meets the Regulations as specified in 21 CFR 208.20
- ensured that the MG meets the criteria as specified in FDA's Guidance for Useful Written Consumer Medication Information (published July 2006)

4 CONCLUSIONS

The MG is 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 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.

Please let us know if you have any questions.

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LYNN M PANHOLZER
03/14/2022 10:17:42 AM

BARBARA A FULLER
03/14/2022 10:23:38 AM

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

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

Memorandum

Date: March 11, 2022

To: Ashley Lane, Regulatory Project Manager
Division of Oncology 2 (DO2)

From: Lynn Panholzer, PharmD, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Emily M. Dvorsky, PharmD, RAC, Team Leader, OPDP

Subject: OPDP Labeling Comments for (b) (4) (penpulimab-xxxx) injection, for intravenous use

BLA: 761258

In response to DO2's consult request dated July 21, 2021, OPDP has reviewed the proposed product labeling (PI), Medication Guide, and carton and container labels for the original BLA submission for (b) (4) (penpulimab-xxxx) injection, for intravenous use.

Labeling: OPDP's comments on the proposed PI are based on the draft PI received by electronic mail from DO2 on March 2, 2022, and are provided below.

A combined OPDP and Division of Medical Policy Programs (DMPP) review of the proposed Medication Guide will be completed, and comments on the proposed Medication Guide will be sent under separate cover.

Carton and Container Labels: OPDP has reviewed the attached proposed carton and container labels submitted by the Applicant to the electronic document room on July 16, 2021, and our comment is provided below.

Thank you for your consult. If you have any questions, please contact Lynn Panholzer at (301) 796-0616 or lynn.panholzer@fda.hhs.gov.

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/s/

LYNN M PANHOLZER
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LABEL AND LABELING REVIEW
Division of Medication Error Prevention and Analysis 2 (DMEPA 2)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

*** This document contains proprietary information that cannot be released to the public***

Date of This Review:	December 20, 2021
Requesting Office or Division:	Division of Oncology 2 (DO2)
Application Type and Number:	BLA 761258
Product Name, Dosage Form, and Strength:	(b) (4) (penpulimab) injection, 100 mg/10 mL (10 mg/mL)
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Akeso Biopharma Co., Ltd.
FDA Received Date:	June 11, 2021; July 16, 2021
OSE RCM #:	2021-1085
DMEPA 2 Safety Evaluator:	Sali Mahmoud, PharmD, BCPS
DMEPA 2 Team Leader:	Ashleigh Lowery, PharmD, BCCCP

1 REASON FOR REVIEW

As part of the approval process for (b) (4) (penpulimab) injection, the Division of Oncology 2 (DO2) requested that we review the proposed (b) (4) prescribing information (PI), container label, and carton labeling for areas of vulnerability that may lead to medication errors.

2 MATERIALS REVIEWED

We considered the materials listed in Table 1 for this review. The Appendices provide the methods and results for each material reviewed.

Table 1. Materials Considered for this Review	
Material Reviewed	Appendix Section (for Methods and Results)
Product Information/Prescribing Information	A
Previous DMEPA Reviews	B
Human Factors Study	C– N/A
ISMP Newsletters*	D – N/A
FDA Adverse Event Reporting System (FAERS)*	E – N/A
Other	F– N/A
Labels and Labeling	G

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 OVERALL ASSESSMENT OF THE MATERIALS REVIEWED

We reviewed the proposed PI, container label, carton labeling, and Medication Guide and determined that they can be improved for clarity and safety.

4 CONCLUSION & RECOMMENDATIONS

The proposed (b) (4) PI, container label, carton labeling, and Medication Guide can be improved for clarity. We provide specific recommendations in Section 4.1 and Section 4.2 below.

4.1 RECOMMENDATIONS FOR DIVISION OF ONCOLOGY 2 (DO2)

A. Prescribing Information

1. Dosage and Administration Section
    a. Section 2.2 Dose Modifications

i. Consider removing the general statement or revise to include withholding for grade 2 reactions to better align with Table 1.
ii. Describe the recommended rate reduction for infusion-related reactions.

b. Section 2.3 Preparation and Administration
i. - Remove the step (b) (4) (b) (4)

c. Consider presenting preparation instructions in a numbered format.

B. Medication Guide

1. Add side effects statement "Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088."

4.2 RECOMMENDATIONS FOR AKESO BIOPHARMA CO., LTD.

We recommend the following be implemented prior to approval of this BLA:

A. General Comments (Container label & Carton Labeling)

1. Revise storage statement to read as: "Must be refrigerated, store at 2°C to 8°C (36°F to 46°F) in original container. Protect from light."
2. Add the product's linear barcode to each individual container and carton as required per 21CFR 201.25(c)(2).
    a. For the container label, ensure that the linear barcode in a vertical position to improve the scannability of the barcode. Barcodes placed in a horizontal position may not scan due to vial curvature.
3. Expiration date format- As currently presented, the format for the expiration date is not defined. To minimize confusion and reduce the risk for deteriorated drug medication errors, identify the 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 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 forward slash or a hyphen be used to separate the portions of the expiration date.
4. The Drug Supply Chain Security Act (DSCSA) requires, for certain prescription products, that the smallest saleable unit display a human-readable and machine-readable (2D data matrix barcode) product identifier. The DSCSA guidance on product identifiers recommends a machine-readable (2D data matrix barcode)

product identifier and a human-readable product identifier. The guidance also recommends the format of the human-readable portion be located near the 2D data matrix barcode as the following:

NDC: [insert NDC]
SERIAL: [insert serial number]
LOT: [insert lot number]
EXP: [insert expiration date]

We recommend that you review the draft guidance to determine if the product identifier requirements apply to your product's labeling. The draft guidance is available from: https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm621044.pdf.[a]

B. Carton Labeling

1. Remove the statement (b) (4) (b) (4) to reduce clutter and redundancy.

[a] When final, this guidance will represent FDA's current thinking on this topic. For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 2 presents relevant product information for [(b) (4)] received on June 11, 2021 from Akeso Biopharma Co., Ltd..

Table 2. Relevant Product Information for [(b) (4)]	
Initial Approval Date	N/A
Active Ingredient	penpulimab
Indication	Nasopharyngral Carcinoma- for the treatment of adult [(b) (4)] with metastatic non-keratinizing nasopharyngeal carcinoma with disease progression on or after platinum-based chemotherapy and at least one other prior line of therapy.
Route of Administration	Intravenous
Dosage Form	injection
Strength	100 mg/10 mL (10 mg/mL)
Dose and Frequency	200 mg administered as an intravenous infusion over 60 minutes every 2 weeks.
How Supplied	[(b) (4)](penpulimab) injection is a sterile, preservative-free, clear to slightly opalescent, colorless to yellowish solution [(b) (4)] [(b) (4)] supplied as: Carton containing one 100 mg/10 mL (10 mg/mL) single-dose vial
Storage	Store [(b) (4)] refrigerated at 2°C to 8°C (36°F to 46°F) in the original carton to protect from light. Do not shake. Do not freeze.
Container Closure	The single-dose vial has a rubber stopper and an aluminum cap with a plastic flip-off disk. Each 10 mL vial is made of [(b) (4)] glass.

APPENDIX B. PREVIOUS DMEPA REVIEWS

On July 12, 2021, we searched for previous DMEPA reviews relevant to this current review using the terms, penpulimab and 761258. Our search identified no previous reviews.

APPENDIX G. LABELS AND LABELING

G.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,[b] along with postmarket medication error data, we reviewed the following (b) (4) labels and labeling submitted by Akeso Biopharma Co., Ltd..

- Container label received on July 16, 2021
- Carton labeling received on July 16, 2021
- Prescribing Information (Image not shown) received on July 16, 2021, available from \\CDSESUB1\evsprod\bla761258\0007\m1\us\114-labeling\114a-draft-label\penpulimab-injection-prescribing-information-text.docx
- Medication Guide received on June 11, 2021, available from \\CDSESUB1\evsprod\bla761258\0004\m1\us\114-labeling\114a-draft-label\penpulimab-injection-medication-guide-text.docx

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

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