CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761352Orig1s000

OTHER REVIEW(S)

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

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

Memorandum

Date: November 18, 2024

To: Maritsa Stephenson, Regulatory Health Project Manager, DO2

Barbara Scepura, Associate Director for Labeling

From: Mispa Ajua-Alemanji, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Rachael Conklin, Team Leader, OPDP

Subject: OPDP Labeling Comments for BIZENGRI (zenocutuzumab-zbco) injection, for intravenous use

BLA: 761352

Background:

In response to DO2's consult request dated March 20, 2024, OPDP has reviewed the proposed product labeling (PI), patient package insert (PPI), and carton and container labeling for the original BLA submission for injection, BIZENGRI (zenocutuzumab-zbco) for intraventricular use (Bizengri).

Labeling: OPDP's comments on the proposed labeling are based on the draft labeling emailed to OPDP on October 28, 2024, and revised labeling accessed on SharePoint on November 16, 2024, and we have no comments at this time.

A combined OPDP and Division of Medical Policy Programs (DMPP) review was completed, and comments on the proposed PPI were sent under separate cover on October 16, 2024.

Carton and Container Labeling: OPDP has reviewed the proposed carton and container labeling submitted by the Sponsor to the electronic document room on September 10, 2024, and our comments are provided below.

Thank you for your consult. If you have any questions, please contact Mispa Ajua-Alemanji at Mispa.Ajua-Alemanji@fda.hhs.gov

Carton and Container Labeling:

Section	**Statement from Draft (if applicable)**	**OPDP Comment**
Front and side panel of Carton label and front panel of vial label.		OPDP recommends revising the established name on the proposed carton and container labeling to be in accordance with 21CFR 201.10(g)(2) which states that, "[t]he established name shall have a prominence commensurate with the prominence with which such proprietary name or designation appears, taking into account all pertinent factors, including typography, layout, contrast, and other printing features." Specifically, we note that the proprietary name is presented in bold dark blue font, whereas the established name is presented in a plain gray font.

23 Page(s) of Draft Labeling have been Withheld in Full as B4 (CCI/TS) immediately following this page

---

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/

MISPA L AJUA-ALEMANJI
11/18/2024 01:05:57 PM

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:	October 16, 2024
To:	Maritsa Stephenson, PharmD, BCPS Regulatory 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)** Laurie Buonaccorsi, PharmD Senior Patient Labeling Reviewer **Division of Medical Policy Programs (DMPP)**
From:	Helen Young, MSN, MPH, CRRN, PHN, RN Patient Labeling Reviewer Position Title **Division of Medical Policy Programs (DMPP)** Mispa Ajua-Alemanji, PharmD Regulatory Review Officer **Office of Prescription Drug Promotion (OPDP)**
Subject:	Review of Patient Labeling: Patient Package Insert (PPI)
Drug Name (established name):	BIZENGRI (zenocutuzumab-zbco)
Dosage Form and Route:	injection, for intravenous use
Application Type/Number:	BLA 761352
Applicant:	Merus N.V. c/o Merus US, Inc.

1 INTRODUCTION

On March 4, 2024, Merus N.V. c/o Merus US, Inc. submitted for the Agency's review an original Biologics Application (BLA) 761352 for BIZENGRI (zenocutuzumab-zbco) injection. The proposed indication for BIZENGRI (zenocutuzumab-zbco) is for the treatment of adult patients with:

- advanced unresectable or metastatic non-small cell lung cancer (NSCLC) harboring a neuregulin 1 (NRG1) gene fusion following progression with prior systemic therapy (b) (4)
- advanced unresectable or metastatic pancreatic adenocarcinoma harboring a neuregulin 1 (*NRG1*) gene fusion following progression with prior systemic therapy (b) (4)

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 March 20, 2024 for DMPP and OPDP to review the Applicant's proposed Patient Package Insert (PPI) for BIZENGRI (zenocutuzumab-zbco) injection.

2 MATERIAL REVIEWED

- Draft BIZENGRI (zenocutuzumab-zbco) injection PPI received on March 4, 2024, and received by DMPP and OPDP on October 4, 2024.
- Draft BIZENGRI (zenocutuzumab-zbco) Prescribing Information (PI) received on March 4, 2024, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on October 4, 2024.
- Approved ENHERTU (fam-trastuzumab deruxtecan-nxki) for injection comparator labeling dated April 5, 2024.

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. We reformatted the PPI document using the Arial font.

In our collaborative review of the PPI we:

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

- ensured that the PPI is free of promotional language or suggested revisions to ensure that it is free of promotional language
- ensured that the PPI meets the criteria as specified in FDA's Guidance for Useful Written Consumer Medication Information (published July 2006)
- ensured that the PPI is consistent with the approved comparator labeling where applicable

4 DISCUSSION

On October 7, 2024, DMPP and OPDP inquired with DO2 whether the Applicant's PPI requires a conversion to a Medication Guide (MG) to reflect the boxed warning in the PI. DO2 indicated that a PPI is sufficient, and therefore, no conversion has been made. Instead, DMPP and OPDP added a "What is the most important information I should know about BIZENGRI? section to the PPI and maintained the order of Warnings and Precautions for consistency with Section 5 of the PI, as directed by DO2.

5 CONCLUSIONS

The PPI is acceptable with our recommended changes.

6 RECOMMENDATIONS

- Please send these comments to the Applicant and copy DMPP and OPDP on the correspondence.
- Our collaborative review of the PPI 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 PPI.

Please let us know if you have any questions.

5 Page(s) of Draft Labeling have been Withheld in Full as B4 (CCI/TS) immediately following this page

---

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/

HELEN K YOUNG
10/16/2024 01:13:08 PM

MISPA L AJUA-ALEMANJI
10/16/2024 01:28:27 PM

LAURIE J BUONACCORSI
10/16/2024 01:33:47 PM

LASHAWN M GRIFFITHS
10/16/2024 01:44:53 PM

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:	September 23, 2024
Requesting Office or Division:	Division of Oncology 2 (DO2)
Application Type and Number:	BLA 761352
Product Name, Dosage Form, and Strength:	Bizengri (zenocutuzumab-zbco) Injection, 375 mg/18.75 mL (20 mg/mL)
Applicant Name:	Merus NV
FDA Received Date:	September 10, 2024
TTT ID #:	2024-8592-1
DMEPA 2 Safety Evaluator:	Janine Stewart, PharmD
DMEPA 2 Team Leader:	Tingting Gao, PharmD

1 PURPOSE OF MEMORANDUM

Merus NV submitted revised container label and carton labeling received on September 10, 2024 for Bizengri. The Division of Oncology 2 (DO2) requested that we review the revised container label and carton labeling for Bizengri (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

Merus NV implemented all our recommendations and we have no additional recommendations at this time.

1 Page(s) of Draft Labeling has been Withheld in Full as B4 (CCI/TS) immediately following this page

[a] Stewart, J. Label and Labeling Review for Bizengri (BLA 761352). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2024 SEP 04. TTT ID: 2024-8592.

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/

JANINE A STEWART
09/23/2024 08:10:52 PM

TINGTING GAO
09/24/2024 05:55:09 AM

Clinical Inspection Summary

Date	September 17, 2024
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	Kristin Wessel, MD, Clinical Reviewer Shruti Gandhy, MD, Clinical Reviewer Amy Barone, MD, Team Leader (CDTL) Division of Oncology 2 (DO2), Office of Oncology Products
BLA #	BLA761352
Applicant	Merus NV
Drug	Zenocutuzumab (MCLA-128)
NME (Yes/No)	Yes
Therapeutic Classification	Anti-HER2 and HER3 Bispecific Antibody
Proposed Indication(s)	Treatment of patients with advanced unresectable or metastatic neuregulin 1 (NRG1) fusion-positive Non-Small Cell Lung Cancer (NSCLC) or NRG1 fusion-positive pancreatic ductal adenocarcinoma (PDAC) following progression with prior systemic therapy (b) (4) (b) (4)
Consultation Request Date	April 23, 2024
Summary Goal Date	September 23, 2024
Action Goal Date	October 23, 2024
PDUFA Date	November 4, 2024

I. OVERALL ASSESSMENT OF FINDINGS AND RECOMMENDATIONS

Clinical data from Study MCLA-128-CL01 were submitted to the Agency in support of Biologic License Application (BLA 761352) for zenocutuzumab (MCLA-128) for the treatment of patients with advanced unresectable or metastatic NRG1 fusion-positive NSCLC or NRG1 fusion-positive PDAC following progression with prior systemic therapy (b) (4) Two clinical investigators, Drs. Alison Schram (Site # 3001), and Koichi Goto (Site # 6001), as well as the (b) (4) Contract Research Organization (CRO), (b) (4), and the study sponsor, Merus NV, were inspected.

Inspections of the CIs, Drs. Schram and Goto, the sponsor, Merus NV, and the (b) (4) CRO, (b) (4) revealed no significant discrepancies or regulatory violations. Based on these inspections, Study MCLA-128-CL01 appears to have been conducted adequately and the

data generated by the inspected clinical investigators and the (b) (4) CRO and submitted by the applicant, Merus NV, appear acceptable in support of the proposed indication.

II. BACKGROUND

Merus NV submitted BLA 761352 seeking approval for zenocutuzumab (MCLA-128) for the above indication based on the efficacy and safety results from Study MCLA-128-CL01, a Phase I/II study of zenocutuzumab in patients with solid tumors. Zenocutuzumab is a new molecular entity (NME), bispecific antibody that binds to the extracellular domains of HER2 and HER3 expressed on the cell surface.

MCLA-128 is an ongoing, open-label, multicenter, multinational study, with a dose-escalation phase followed by a single-arm, multiple-indication expansion group assignment phase. The Phase 1 portion of the study evaluated escalating doses of zenocutuzumab from 40 to 900 mg administered every 3 weeks (Q3W). The Phase 2 portion enrolled patients with non-NRG1 positive and NRG1 positive patients with various tumors in expansion cohorts (Group A thru Group H).

Data submitted to support BLA 761352 consists of subjects with NRG1+ tumors enrolled in Group F (NRG1+ non-small cell lung cancer [NSCLC]), Group G (NRG1+ pancreatic ductal adenocarcinoma [PDAC], or Group H (other NRG1+ solid tumors). As of Protocol Amendment 5.0, the expansion part of the study focused exclusively on patients with advanced unresectable or metastatic NRG1+ cancer, and the study was thereafter named the "eNRGy study".

Subjects who met all study eligibility criteria received zenocutuzumab 750 mg administered as an intravenous (IV) infusion every 2 weeks until unacceptable toxicity or disease progression.

Eligible patients must sign the informed consent before undergoing any protocol-specific procedures. Standard laboratory tests included hematology, coagulation, chemistry panels, and urinalysis. ECG and left ventricular ejection fraction (LVEF) assessment were to be performed at screening within 28 days of initiation of study treatment and at protocol specified time points. Radiological tumor assessment (CT and/or MRI) were to be performed at screening, then every 8 weeks until disease progression. Patients who did not have disease progression had their disease status assessed every 3 months, for a maximum of 2 years.

The primary efficacy endpoints were confirmed overall response rate (ORR) and duration of response (DOR) as determined by blinded independent central review (BICR) according to RECIST v1.1.

At the time of the data cut-off date of July 31, 2023, the study enrolled a total of 175 NRG1 fusion-positive cancer patients, including 99 subjects with NRG1positive NSCLC, 99 subjects with NRG1positive PDAC, and 37 with other NRG1 positive solid tumor types. Data from 64 subjects NSCLC previously treated with systemic therapy, 11 subjects with treatment-naïve

NSCLC, and 29 subjects with advanced PDAC were submitted to support the proposed indications.

III. RESULTS (by site):

1. **Dr. Alison Schram (Site # 3001)**
   1275 York Ave
   New York, NY 10065-6007
   USA

   Inspection dates: June 4 – 11, 2024.

   Dr. Schram was inspected as a routine PDUFA inspection for Study MCLA-128-CL01. This was the first FDA inspection for this investigator.

   At the time of the inspection, the site had screened 18 subjects and had enrolled 17 subjects in the study. Of the 17 subjects enrolled, 3 subjects were still on active treatment, 2 subject were in follow-up phase, and 12 subjects had completed the study.

   Source records for all 17 subjects enrolled in the study were reviewed. Records reviewed included: informed consent forms, inclusion and exclusion criteria, investigational drug administration, adverse events reporting, protocol deviations, and subject dispositions. Records were compared with datasets and listings submitted to the BLA. No significant discrepancies were observed between source records and data listings.

   The inspection also verified that study procedures related to tumor assessment were performed according to the protocol and that all radiographic scans were submitted for central review. Source records confirmed that procedures were performed per protocol. No discrepancies were observed when compared to the data submitted to the BLA.

   Additional records reviewed included but were not limited to: Institutional Review Board (IRB) correspondence and approvals, staff training, monitoring records, financial disclosures, and investigational drug storage and accountability records.

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

2. **Dr. Koichi Goto (Site # 6001)**
6-5-1 Kashiwanoha
Kashiwa-Shi NA 27708577
Japan

Inspection dates: July 16 - 19, 2024.

Dr. Goto was inspected as a routine PDUFA inspection for Study MCLA-128-CL01. This was the first FDA inspection for this investigator.

At the time of the inspection, the site had screened 54 and had enrolled 14 subjects in the study, of these 2 subjects were still active on study, 3 subjects were in follow-up phase, and 9 subjects had discontinued study due to disease progression.

The inspection reviewed records for 12 enrolled subjects in full and compared with data listings submitted to the BLA. Records reviewed included informed consent forms, eligibility criteria, adverse events reporting, concomitant medications, laboratory tests, echocardiogram, and ECGs. There were no unreported protocol deviations noted during the conduct of the inspection and source documents were in general consistent with the data listing submitted to the BLA. Radiographic images for tumor assessment were performed at protocol specified time points and all scans were submitted for central review.

Additional records reviewed during the inspection included, but were not limited to, IRB correspondence and approvals, financial disclosure forms, monitoring procedures, staff training, monitoring records, sponsor correspondence, and investigational product storage records and accountability. No regulatory violations were observed.

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

3. **Merus N.V. (Sponsor)**
Fortrea (CRO)
5 Roxborough Way
Maidenhead SL6 3UD
United Kingdom

Inspection dates: July 15 – 25, 2024. This inspection assessed Merus' oversight responsibilities for MCLA-128-CL01 study. This was the first BIMO inspection for this Sponsor.

The inspection took place at Fortrea, a CRO, where the MCLA-128-CL01 study paper trial master files were maintained. Documents reviewed included, but were not limited to, clinical investigators selection, FDA1572 forms, financial records, monitoring process and reports, IRB approvals, informed consent documents, written procedures,

investigational product accountability and vendor agreements. In addition, Data Review Committee (DRC) charter and meeting minutes, were also reviewed.

The study's safety and adverse event management plan, reporting, and electronic system used were also reviewed. Adverse event listings on the electronic system were compared with the AEs reported by the clinical sites on the electronic capture (EDC system) for randomly selected subjects. No discrepancies were noted.

The inspection did not observe issues with the clinical investigator and staff selection processes, qualifications, training, or compliance with the investigational plan. No issues related to safety/adverse event handling or reporting for MCLA-128-CL01 were observed.

Based on the results of the inspection, Merus' overall oversight of the study and monitoring of the clinical investigators appear adequate.

4. (b) (4) **CRO)**
(b) (4)

Inspection dates: (b) (4)

(b) (4) was inspected as a routine PDUFA inspection for Study MCLA-128-CL01. The firm was previously inspected in (b) (4)
(b) (4)

This inspection reviewed (b) (4) responsibilities to perform an independent central (b) (4) review for Study MCLA-128-CL01. Records reviewed included, but were not limited to, (b) (4) procedures regarding the (b) (4)
(b) (4).
The review found the processes adequate.

(b) (4)
(b) (4) No discrepancies were observed. The ID of these subjects are as follow:

Subject ID		
Group F (NSCLC)		Group G (PDAC)
Previous Treatment	Treatment Naive	
(b) (6)		

Additional documents reviewed during the inspection included: (b) (4) (b) (4) (b) (4) No issues were observed.

Based on the results of the inspection, the (b) (4) review data generated by (b) (4) (b) (4) 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:

{See appended electronic signature page}

Michele Fedowitz, M.D.
Team Leader
Good Clinical Practice Assessment Branch
Division of Clinical Compliance Evaluation
Office of Scientific Investigations

CONCURRENCE: {*See appended electronic signature page}*

Jenn Sellers, M.D., Ph.D.
Branch Chief
Good Clinical Practice Assessment Branch
Division of Clinical Compliance Evaluation
Office of Scientific Investigations

CC:

Review Division /Project Manager/Maritsa Stephenson
OSI/DCCE/GCPAB/Program Analyst/Yolanda Patague

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/

LEE HONG PAI SCHERF
09/17/2024 11:48:14 AM

MICHELE B FEDOWITZ
09/17/2024 11:52:37 AM

JENN W SELLERS
09/17/2024 11:54:20 AM

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:	September 4, 2024
Requesting Office or Division:	Division of Oncology 2 (DO2)
Application Type and Number:	BLA 761352
Product Name, Dosage Form, and Strength:	Bizengri (zenocutuzumab-zbco) Injection, 375 mg/18.75 mL (20 mg/mL)
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant Name:	Merus NV
FDA Received Date:	March 4, 2024
TTT ID #:	2024-8592
DMEPA 2 Safety Evaluator:	Janine Stewart, PharmD
DMEPA 2 Acting Team Leader:	Tingting Gao, PharmD

1 INTRODUCTION

As part of the approval process for Bizengri (zenocutuzumab-zbco) Injection, the Division of Oncology 2 (DO2) requested that we review the proposed Bizengri Prescribing Information (PI), Patient Package Insert (PPI), container label, and carton labeling for areas of vulnerability that may lead to medication errors.

2 MATERIALS REVIEWED

This section lists the materials considered for our review of BLA 761352.

Table 1. Materials Considered for this Label and Labeling Review	
Material(s) Reviewed	Appendix Section
Relevant Product Information	A
Labels and Labeling	B

3 CONCLUSION

We evaluated the proposed Bizengri Patient Package Insert (PPI), and determined that it is acceptable from a medication error perspective.

However, the proposed Bizengri Prescribing Information (PI), container label, 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 Merus NV in Section 5.

4 RECOMMENDATIONS FOR THE DIVISION OF ONCOLOGY 2 (DO2)

A. Prescribing Information

1. Section 2 Dosage and Administration

   a. In Section 2.5 *Preparation*, consider deleting the statement (b) (4) (b) (4)

   b. Given the short stability of BIZENGRI infusion (6 hours), the recommended duration of initial infusions of 4 hours, and the risk for infusion-related-reactions which might require extending the infusion time, consider adding the following statement at the beginning of Section 2.5 *Preparation*:

      > For the initial infusion, prepare BIZENGRI as close to administration time as possible to allow for the possibility of extended infusion time in the event of an infusion related reaction.

c. Consider revising for clarity the statement regarding storage of the diluted solution if it is not used within 2 hours of preparation to read "If not used immediately, store the diluted solution refrigerated at 2°C to 8°C (36°F to 46°F) after preparation unless the infusion is initiated within 2 hours of preparation."

d. Consider relocating and revising the statement that reads (b) (4)

(b) (4)

e. For improved readability, consider revising the format of Section 2.5 and Section 2.6 to present the preparation and administration information using bullets as follows:

2.5 Preparation

Dilute and prepare BIZENGRI for intravenous infusion before administration.

For the initial infusion, prepare BIZENGRI as close to administration time as possible to allow for the possibility of extended infusion time in the event of an infusion-related reaction.

- Check that the BIZENGRI solution is colorless to slightly yellow. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Do not use if discoloration or visible particles are present.
- Withdraw and then discard 37.5 mL 0.9% Sodium Chloride Injection from the 250 mL infusion bag. Only use infusion bags made of polyvinylchloride (PVC), polyolefin or polyolefin/polyamide coextruded plastic.
- Withdraw a total of 37.5 mL of BIZENGRI from 2 vials and add it to the infusion bag. The final volume in the infusion bag should be 250 mL. Discard any unused portion left in the vial.
- Gently invert the bag to mix the solution. Do not shake.
- If not used immediately, store the diluted solution refrigerated at 2°C to 8°C (36°F to 46°F) after preparation unless the infusion is initiated within 2 hours of preparation.

2.6 Administration

- Administer diluted BIZENGRI solution within x hours (including infusion time) following storage at room temperature at 15°C to 25°C (59°F to 77°F), or within 24 hours (including infusion time) following refrigeration at 2°C to 8°C (36°F to 46°F). If the

diluted BIZENGRI solution has been refrigerated, allow it to reach room temperature (approximately 30 minutes) prior to administration.

- Administer diluted BIZENGRI solution *[see Dosage and Administration (0)]* by intravenous infusion using an infusion set (b) (4) with an in-line, sterile, non-pyrogenic, low protein-binding polyethersulfone (PES) filter (pore size 0.2 micrometer).

- Administration sets must be made of either PVC, polyethylene (PE), polyurethane (PUR) or polybutadiene (PB).

- Do not infuse BIZENGRI concomitantly in the same IV line with other agents.

- Administer BIZENGRI infusion via a peripheral or central line.

(b) (4)

2. Section 3 Dosage Forms and Strengths
    a. As proposed, the strength statement does not express the total strength per total volume. Revise the strength to read "375 mg/18.75 mL (20 mg/mL)

5 RECOMMENDATIONS FOR MERUS NV

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

1. As currently presented, the artistic presentation of the letter “ri” at the end of the proprietary name, Bizengri, may be misinterpreted as the letter “n”. We recommend you reconsider the font or styling used in the presentation of the proprietary name to reduce the risk of misinterpretation of the proprietary name, Bizengri.
2. As proposed, the strength statement does not express the total strength per total volume. Revise the strength to read "375 mg/18.75 mL (20 mg/mL) per vial*".
3. We recommend revising the statement (b) (4) (b) (4) to read “For Intravenous Infusion After Dilution”. We recommend this revision because (b) (4) (b) (4)

B. Container label

1. As proposed, the package-type term is incorrect. Revise the package-type term that reads (b) (4) to read "single-dose vial".
2. To reduce clutter on the side panel, remove the strength statement “375 mg/18.75 mL (20 mg/mL)” and relocate the “Discard unused portion.” so that it appears after the package-type term. For example. “Single-dose vial. Discard unused portion.”

C. Carton labeling

1. Consider removing the NDC statement “Contains 2 of NDC 83077-100-01” to minimize confusion regarding the NDC number for the carton.
2. As proposed, the package-type term is incorrect. Revise the package-type term that reads (b) (4) to read "single-dose vials".
3. Revise as follows the net quantity statement and, where it appears, the graphic used to depict that 2 vials are needed to achieve the recommended 750 mg dose:

*Each carton contains:
Two 375 mg/18.75 mL single-dose vials. Discard unused portion.

 = one 750 mg dose

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. RELEVANT PRODUCT INFORMATION

Table 2 presents relevant product information for Bizengri received on March 4, 2024 from Merus NV.

Table 2. Relevant Product Information for Bizengri	
Initial Approval Date	N/A
Nonproprietary Name	zenocutuzumab-zbco
Indication	BIZENGRI is indicated for adult patients with advanced unresectable or metastatic non-small cell lung cancer (NSCLC) harboring a neuregulin 1 (NRG1) gene fusion following progression with prior systemic therapy (b) (4) (b) (4)
Dosage Form	Injection
Strength	375 mg/18.75 mL (20 mg/mL)
Route of Administration	Intravenous Infusion
Dose and Frequency	750 mg intravenously every 2 weeks
How Supplied	Two single-dose vials per carton
Storage	Store in a refrigerator at 2°C to 8°C (36°F to 46°F) in original carton to protect from light. Do not freeze. Do not shake.
Container Closure	(b) (4) type (b) (4) single- (b) (4) vials closed with a (b) (4) rubber stopper (b) (4) and secured with an aluminum seal with flip-off cap.

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,[a] along with postmarket medication error data, we reviewed the following Bizengri labels and labeling submitted by Merus NV.

- Prescribing Information and Patient Package Insert received on March 4, 2024, available from \\CDSESUB1\EVSPROD\bla761352\0003\m1\us\114-labeling\114a-draft-label\proposed-uspi-bizengri.docx
- Container label(s) received on March 4, 2024
- Carton labeling received on March 4, 2024

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

Container label(s)

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

1 Page(s) of Draft Labeling has been Withheld in Full as B4 (CCI/TS) immediately following this page

---

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/

JANINE A STEWART
09/04/2024 10:09:50 AM

TINGTING GAO
09/04/2024 12:58:47 PM