CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761263Orig1s000

OTHER REVIEW(S)

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

PATIENT LABELING REVIEW

Date:	December 2, 2022
To:	Kimberly Scott, RN, BSN, OCN® Regulatory Project Manager **Division of Hematologic Malignancies II (DHM2)**
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:	Laurie Buonaccorsi, PharmD Patient Labeling Reviewer **Division of Medical Policy Programs (DMPP)** Jennifer Chen, PharmD, MBA Regulatory Review Officer **Office of Prescription Drug Promotion (OPDP)**
Subject:	Review of Patient Labeling: Medication Guide (MG)
Drug Name (established name):	LUNSUMIO (mosunetuzumab-axgb)
Dosage Form and Route:	injection, for intravenous use
Application Type/Number:	BLA 761263
Applicant:	Genentech, Inc.

1 INTRODUCTION

On April 29, 2022, Genentech, Inc. submitted for the Agency's review an original Biologics License Application (BLA) 761263 for LUNSUMIO (mosunetuzumab-axgb) injection. The proposed indication for LUNSUMIO (mosunetuzumab-axgb) injection is for the treatment of adult patients with relapsed or refractory follicular lymphoma who have received at least two prior systemic therapies.

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 Hematologic Malignancies II (DHM2) on June 30, 2022 for DMPP and OPDP to review the Applicant's proposed Medication Guide (MG) for LUNSUMIO (mosunetuzumab-axgb) injection.

2 MATERIAL REVIEWED

- Draft LUNSUMIO (mosunetuzumab-axgb) injection MG received on April 29, 2022 and received by DMPP and OPDP on November 18, 2022.
- Draft LUNSUMIO (mosunetuzumab-axgb) injection Prescribing Information (PI) received on April 29, 2022, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on November 18, 2022.
- Approved TECVAYLI (teclistamab-cqyv) and BLINCTYO (blinatumomab) comparator labeling dated October 25, 2022 and February 18, 2022, respectively.

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

- ensured that the MG meets the criteria as specified in FDA's Guidance for Useful Written Consumer Medication Information (published July 2006)
- ensured that the MG is consistent with the approved comparator labeling where applicable

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: 11/28/22

To: Kimberly Scott, RN, BSN, OCN
Senior Regulatory Health Project Manager
Division of Hematological Malignancies II (DHM2)

From: Jennifer Chen, PharmD, MBA, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Jina Kwak, PharmD, RAC, Team Leader, OPDP

Subject: OPDP Labeling Comments for LUNSUMIO™ (mosunetuzumab-axgb) injection, for intravenous use

BLA: 761263

Background:
In response to DHM2's consult request dated September 27, 2021, OPDP has reviewed the proposed Prescribing Information (PI) and Medication Guide for the original BLA submission for LUNSUMIO™ (mosunetuzumab-axgb) injection, for intravenous use.

PI/Medication Guide:
OPDP's review of the proposed PI is based on the draft labeling emailed to OPDP on November 18, 2022, and our comments are provided below.

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

Thank you for your consult. If you have any questions, please contact Jennifer Chen at (301) 796-9398 or Jennifer.Chen@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)

Date of This Memorandum:	November 16, 2022
Requesting Office or Division:	Division of Hematologic Malignancies 2 (DHM 2)
Application Type and Number:	BLA 761263
Product Name and Strength:	Lunsumio (mosunetuzumab-axgb) Injection, 1 mg/mL, 30 mg/30 mL (1 mg/mL)
Applicant/Sponsor Name:	Genentech, Inc.
OSE RCM #:	2021-1566-1
DMEPA 2 Safety Evaluator:	Nicole Iverson, PharmD, BCPS
DMEPA 2 Team Leader:	Hina Mehta, PharmD

1 PURPOSE OF MEMORANDUM

The Applicant submitted revised container labels and carton labeling received on September 21, 2022 and November 10, 2022 for Lunsumio. We reviewed the revised container labels and carton labeling for Lunsumio (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 in addition to recommendations made by the Office of Biotechnology Products labeling.[a]

2 CONCLUSION

The Applicant implemented all of our recommendations and we have no additional recommendations at this time.

[a] Iverson, N. Label and Labeling Review for Lunsumio (BLA 761263). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2022 SEP 12. RCM No.: 2021-1566.

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CLINICAL INSPECTION SUMMARY

Date	October 27, 2022
From	Anthony Orencia M.D., F.A.C.P., Medical Officer Min Lu, M.D., M.P.H., Team Leader Jenn Sellers, M.D., Ph.D., F.A.A.P., Acting Branch Chief Good Clinical Practice Assessment Branch Division of Clinical Compliance Evaluation Office of Scientific Investigations
To	Pamela Seam, M.D., Medical Officer Nicholas Richardson, D.O., M.P.H., Medical Team Leader Nicole Gormley, M.D., Division Director Kimberly Scott, RN, BSN, OCN®, Senior Regulatory Health Project Manager Division of Hematology Malignancies 2 (DHM2) Office of Oncology Drugs
BLA	BLA 761263
Applicant	Genentech, Inc.
Drug	Sunlumio™ (mosunetuzumab)
NME	Yes
Division Classification	Anti-CD20/CD3 T-cell dependent bispecific antibody
Proposed Indication	Treatment of adult patients with relapsed or refractory follicular lymphoma who have received at least two prior systemic therapies.
Review Type	Priority Review
Consultation Request Date	June 6, 2022
Summary Goal Date	November 1, 2022
Action Goal Date	December 1, 2022
PDUFA Date	December 29, 2022

I. OVERALL ASSESSMENT OF FINDINGS AND RECOMMENDATIONS

Clinical data from Study GO29781 were submitted to the Agency in support of a Biologics License Application (BLA) for the drug mosunetuzumab, proposed as treatment of adult patients with relapsed or refractory follicular lymphoma who have received at least two prior systemic therapies. Two clinical investigators (Nancy Bartlett, M.D. and Lihua Elizabeth Budde, M.D.) and the sponsor, Genentech, Inc., were inspected.

Based on the aforementioned inspections, the study data derived from the two clinical investigator sites are considered reliable. The sponsor's oversight and monitoring of Study GO29781 appear adequate. The study data submitted to the Agency for assessment appear acceptable in support of the proposed indication.

II. BACKGROUND

Mosunetuzumab (RO7030816; BTCT4465A) is a humanized anti-CD20/CD3 T-cell dependent bispecific antibody of an immunoglobulin G1 isotype that is produced using the knobs-into-holes technology. One fragment antigen-binding region of the antibody is directed against the extracellular domain of the CD3 epsilon subunit of the T cell receptor complex, and the other Fab region is directed against the extracellular domain of CD20.

Mosunetuzumab as a single agent is proposed for the treatment of adult patients with relapsed or refractory follicular lymphoma (FL) who have received at least two prior systemic therapies.

A single clinical investigation study was submitted in support of the current applicant's BLA.

Study GO29781

Study GO29781 is an ongoing Phase I/II, multicenter, open-label, dose-escalation and dose-expansion study of mosunetuzumab administered as a single agent and in combination with atezolizumab in patients with relapsed/refractory hematologic malignancies expected to express CD20, including B-cell non-Hodgkin's lymphoma and chronic lymphocytic leukemia.

In the dose-escalation stage in non-Hodgkin's lymphoma patients, five dose-escalation groups are evaluating the safety, tolerability, and pharmacokinetics of mosunetuzumab either as a single agent administered by different dosing schedules and routes of administration (intravenous infusion [Groups A and B] or by subcutaneous injection [Group D and F]), or in combination with atezolizumab (intravenous infusion [Group E]).

In the dose expansion stage of the study, further assessment of mosunetuzumab clinical activity and safety as a single agent and in combination with atezolizumab is being conducted in separate indication-specific expansion cohorts of patients with relapsed/refractory follicular lymphoma, diffuse large B cell lymphoma/transformed follicular lymphoma, mantle cell lymphoma) and Richter's transformation. Each indication specific expansion cohort was to test doses at or below the maximum tolerated dose from the dose escalation phase, including the recommended Phase II dose.

In Group A (and Group D), mosunetuzumab was to be administered as a fixed dose on Day 1 of each 21-day cycle. In Group B (and Group F) mosunetuzumab was to be administered by a Cycle 1 step-up dosing schedule whereby in each dose level cohort, increasing doses were administered on Days 1, 8 and 15 of Cycle 1 only of a every three-week schedule.

The escalation cohorts consisted of the following: (A) fixed-dose schedule: 33 patients with relapsed/refractory non-Hodgkin's lymphoma in Group A in 8 dose escalation cohorts, and (B) Step-up dose schedule: 414 patients with relapsed/refractory B-cell non-Hodgkin's lymphoma in Group B in 11 dose escalation cohorts (B1-B11) and two major dose expansion cohorts; B7: a dose level initially evaluated as a putative recommended Phase II dose; referred to as the interim dose; 1/2/13.5 mg) and the higher B11 dose level selected as the final recommended Phase 2 Dose (1/2/60/30 mg).

Mosunetuzumab was administered for 8 cycles (for patients who achieved a complete response after 8 cycles) or up to 17 cycles (for patients who achieved a partial response or maintained stable disease after 8 cycles), unless progressive disease or unacceptable toxicity was observed as the duration of therapy.

The primary safety endpoints comprise the incidence and nature of drug limiting toxicities in dose escalation phase, the incidence, nature, and severity of adverse events, the incidence of cytokine release syndrome, as well as interventions for cytokine release syndrome, the incidence of adverse events leading to mosunetuzumab dose modifications, changes in vital signs and clinical laboratory values, the incidence of electrocardiographic abnormalities, and the incidence of anti-drug antibodies.

The primary efficacy endpoint (for relapsed/refractory follicular lymphoma and diffuse large B cell lymphoma/transformed follicular lymphoma expansion cohorts) was independent review facility-assessed complete response, defined as the proportion of patients whose best overall response was a complete response using standard criteria for non-Hodgkin's lymphoma.

Study GO29781 enrolled patients in the following countries: United States (15 sites), Australia, Canada, Republic of Korea, Spain, Germany and United Kingdom. The first study patient enrolled on September 15, 2015. The data cut-off for analyses was August 27, 2021.

This Phase I/II study is ongoing.

III. RESULTS

1. Nancy Bartlett, M.D./Site: 284510
Washington University School of Medicine in St. Louis
660 S Euclid Ave
St. Louis, MO 63110

Inspection dates: June 21 to 28, 2022

At Dr. Bartlett's Site 284510, 90 were screened, and 68 study subjects were enrolled. Of those enrolled in this Phase I/II clinical investigation, 38 were on treatment or in follow-up. For this ongoing study, there were 17 enrolled study subjects who completed treatment at the time of the inspection.

The inspection reviewed subject eligibility, protocol adherence, adverse event evaluation and reporting, safety assessments and drug accountability, Institutional Review Board (IRB) approval letters and correspondence, informed consent forms, monitoring reports, financial disclosure reports, site signature and responsibility logs and site training documentation. Source records also comprised a review of study specific case report forms (CRF), electronic laboratory results, progress and nurse notes, electrocardiogram printouts, imaging scan results both in paper and electronically, and study subject requisition forms. The e-CRF system used for this study was RAVE Medidata.

A total of 25 study subjects' records were reviewed during the inspection for enrolled subjects, under Cohort A, B, D, E and F as mentioned above. Study subject data line listings were compared to source documents. No discrepancies were reported.

The primary efficacy endpoint (complete response) was verifiable during the study site inspections. Records were also assessed for adverse events. No underreporting for adverse and serious adverse events were found at Dr. Bartlett's study site.

A Form FDA 483 (Inspectional Observations) was not issued at the end of the site inspection.

2. Lihua Elizabeth Budde, M.D. / Site: 284773
City of Hope Comprehensive Center
1500 E Duarte Rd
Duarte, CA 91010

Inspection dates: July 11 to 15, 2022

At Dr. Budde's Site 284773, a total of 134 subjects were screened, and 100 subjects were enrolled to participate in the study. Of the 100 subjects enrolled, 51 terminated early due to disease progression (death) or physician's decision. This Phase I/II study is ongoing with only a single subject currently on-treatment.

The following documents and study site activities were assessed: protocol adherence, subject inclusion and exclusion criteria, adverse event evaluation and reporting, safety assessments and drug accountability, IRB approval letters and correspondence; monitoring reports, informed consent forms, subject medical histories, financial disclosure reports, electronic and paper case report forms, site signature and responsibility logs and site training documentation. Raw clinical data line listings were compared to source documents.

A total of 25 enrolled subjects' source and electronic records, from groups A, B, D, E and F as described above, were assessed. There were no discrepancies found when study subject data line listings were compared to source documents at Dr. Budde's clinical site.

Source records evaluated were verifiable for primary endpoint data. There was no evidence of under-reporting of adverse events.

The inspection was unremarkable in general. No FDA Form 483 (Inspectional Observations) was issued at the end of the inspection.

3. Genentech, Inc./ Sponsor

1 DNA Way
South San Francisco, CA 94080-4990

Inspection dates: September 29 to October 7, 2022

During the FDA inspection of the sponsor, an evaluation of the clinical trial overview was performed and comprised the following activities: sponsor oversight, clinical investigator site and monitor selection, record collection (e.g., financial disclosures, Form FDA 1572), electronic records and electronic signatures, monitoring activities by the sponsor and site monitors quality assurance, safety assessments, adverse event reporting, blinding (e.g., blinding of clinical trial staff, site monitors, biostatisticians, investigational product), investigational product (i.e., distribution and blinding), transfer of regulatory obligations, contractual agreements site monitoring (i.e., procedure, monitoring reports, frequency or qualification of monitors), and electronic data capture (i.e., validation, user acceptance testing, audit trail).

There were five clinical sites whose clinical trial compliance activities were assessed. Significant protocol deviations were reported to this sponsor, and appropriate corrective actions were completed for the investigator sites. Monitoring actions taken for those clinical investigators who did not comply with the investigational plan appeared to be adequate. Adverse events were comprehensively reported to the Agency.

At the end of the sponsor inspection, no FDA Form 483 was issued.

In general, the sponsor oversight and monitoring of this clinical study appear to be acceptable.

{See appended electronic signature page}
Anthony Orencia, M.D., Ph.D.
Good Clinical Practice Assessment Branch
Division of Clinical Compliance Evaluation
Office of Scientific Investigations

CONCURRENCE:

{See appended electronic signature page}
Min Lu, M.D., M.P.H.
Team Leader
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CONCURRENCE:

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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:	September 12, 2022
Requesting Office or Division:	Division of Hematologic Malignancies 2 (DHM 2)
Application Type and Number:	BLA 761263
Product Name, Dosage Form, and Strength:	Lunsumio (mosunetuzumab-axgb) Injection, 1 mg/mL, 30 mg/30 mL (1 mg/mL)
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Genentech, Inc.
FDA Received Date:	December 28, 2021, April 29, 2022, August 10, 2022, and September 6, 2022
OSE RCM #:	2021-1566
DMEPA 2 Safety Evaluator:	Nicole Iverson, PharmD, BCPS
DMEPA 2 Team Leader:	Hina Mehta, PharmD

1 REASON FOR REVIEW

As part of the approval process for Lunsumio (mosunetuzumab-axgb) Injection, this review evaluates the proposed Lunsumio Prescribing Information (PI), Medication Guide, container labels, 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 – N/A
Human Factors Study	C – N/A
ISMP Newsletters*	D – N/A
FDA Adverse Event Reporting System (FAERS)*	E – N/A
Other	F
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

Genentech, Inc. submitted a 351(a) application to obtain marketing approval of Lunsumio (mosunetuzumab-axgb) Injection. Lunsumio is proposed for the treatment of adult patients with relapsed or refractory follicular lymphoma who have received at least two prior systemic therapies.

We performed a risk assessment of the proposed container labels, carton labeling, PI, and Medication Guide for Lunsumio Injection to determine whether there are significant concerns in terms of safety related to preventable medication errors. We note the Applicant will provide a peel-off sticker, "Do not use in-line filter", that appears at the end of the Medication Guide and should be applied to the infusion bag prior to administration. Since the sticker is attached to the end of the Medication Guide, we sent an Information Request for a 3D image mock-up of how the sticker will appear. Additionally, we requested the rationale for the peel-off sticker, the clinical consequence that may occur if an in-line filter is used during administration of the

product, and if there were any administration errors observed during your clinical study using a filter. The Applicant responded on September 6, 2022 with images of the peel-off sticker on the outside of the folded carton labeling insert. The Applicant asserted that the proposed product should not be administered using an in-line filter because of protein binding to the in-line filter, which could result in underdosing. Additionally, the Applicant noted use errors observed during the clinical study and human factors testing with the proposed peel-off sticker as risk mitigation strategy to prevent administration errors with the product.[a] See Appendix F for full information request.

We note the dosage form in the PI is not consistent with USP General Chapter <1121> nomenclature and we defer to the Office of Biotechnology Products (OBP) for the correct nomenclature for the dosage form. The proposed Medication Guide is acceptable from a medication error perspective. We identified areas of the proposed labels and labeling that could be revised to improve clarity and readability of important information. For the Division, we note lack of clarity in the recommended dosage, preparation and storage instructions. We also note abbreviations for the route of administration and negative statements. For the Applicant, we note that the Rx only statement appears bolded, the expiration date format is undefined, and the net quantity statement is missing. In addition, the proprietary name is presented with the placeholder, "TRADENAME". These factors may confuse the user and inadvertently lead to medication errors. We provide recommendations for the Division in Section 4.1 and the Applicant in Section 4.2 to address these deficiencies.

4 CONCLUSION & RECOMMENDATIONS

The proposed Medication Guide is acceptable from a medication error perspective. We identified areas in the proposed container labels, carton labeling, and PI that can be improved to increase readability and prominence of important information and promote the safe use of the product. We provide recommendations in Section 4.1 for the Division and Section 4.2 for Genentech, Inc. to address our concerns.

4.1 RECOMMENDATIONS FOR DIVISION OF HEMATOLOGIC MALIGNANCIES 2 (DHM 2)

A. Highlights of Prescribing Information

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[a]Lunsumio Injection 1 mg/mL, 30 mg/30 mL. BLA Number: BLA 761263, Sequence Number: 0044. DMEPA 2 INFORMATION REQUEST. South San Francisco (CA): Genentech, Inc. 2022 SEP 06. Available from \\CDSESUB1\EVSPROD\bla761263\0044\m1\us\20220906-response.pdf

1. Dosage and Administration

    a. The warning statement, [redacted] is expressed as a negative statement. [redacted] we recommend removing the statement [redacted].

    b. Lunsumio has different preparation instructions depending upon the cycle and recommended dosage. Therefore, we recommend including the statement, "See Full Prescribing Information for instructions on preparation and administration. (2.5)."

B. Prescribing Information

1. Dosage and Administration Section

    a. Section 2.1 Important Dosing Information

        i. The warning statement, [redacted] is expressed as a negative statement. [redacted], we recommend removing the fourth bulleted statement [redacted].

    b. Section 2.2 Recommended Dose

        i. We recommend revising the title from, [redacted] to "Recommended Dosage" to align with current labeling terminology.

        ii. As currently presented, the dose interruption schedule lacks clarity due to the layout in which the information is presented. Therefore, we recommend incorporating the text into a table for added clarity as follows:

        Table 1: Recommendations for restarting therapy with LUNSUMIO after dose delay

        [redacted]

Table 1: Recommendations for restarting therapy with LUNSUMIO after dose delay

(b) (4)

c. Section 2.3 Recommended Premedication and Prophylactic Medications
    i. The route of administration is abbreviated as "IV". Presenting the route of administration as an abbreviation may lead to misinterpretation of the correct route of administration. We recommend revising all presentations of "IV" to "Intravenous".
    ii. The unit of measure is missing in the dose ranges for premedications. We recommend revising the premedication dose ranges to include the unit of measure after each dose range (e.g. Diphenhydramine hydrochloride 50 mg to 100 mg or equivalent oral or intravenous anti-histamine).
    iii. The strength of acetaminophen is presented as a large number and appears without comma(s) to improve readability. Numbers greater than or equal to 1,000 should contain a comma to prevent the reader from misinterpreting thousands "1000" as hundreds "100" or ten-thousands "10000". We recommend revising the strength statement to include a comma, for example, to read as 1,000 instead of 1000.

d. Section 2.5 Preparation and Administration
    i. The preparation instructions lack clarity, which may lead to product preparation errors. Therefore, we recommend the following revisions:
        a. Revise all instances of (b) (4) to appear using correct nomenclature, "0.9% Sodium Chloride Injection, USP or 0.45% Sodium Chloride Injection, USP".
        b. <u>Preparation</u>

            Use aseptic technique to prepare LUNSUMIO.

- Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Do not use if the solution is discolored, or cloudy, or if foreign particles are present.
- Determine the dose, the total volume of LUNSUMIO solution required, and the number of LUNSUMIO vials needed.
- Withdraw the volume from an infusion bag of 0.9% Sodium Chloride Injection, USP or 0.45% Sodium Chloride Injection, USP equal to the volume of the LUNSUMIO required for the patient's dose and discard. Only use infusion bags made of polyvinyl chloride (PVC) or polyolefin (PO) such as polyethylene (PE) and polypropylene infusion bag.
- Withdraw the required volume of LUNSUMIO from the vial and dilute into 100 mL infusion bag of 0.9% Sodium Chloride Injection, USP or 0.45% Sodium Chloride Injection, USP. Discard any unused portion left in the vial.
- Gently mix the intravenous bag by slowly inverting the bag. *Do not shake.*
- Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Do not use if visibly opaque particles, discoloration or foreign particles are observed.
- Apply the peel-off label from the carton labeling insert to the infusion bag.
- Immediately use diluted LUNSUMIO infusion solution. If not used immediately, the diluted solution can be stored refrigerated at 2°C to 8°C (36°F to 46°F) for up to 24 hours and at ambient temperature 9°C to 30°C (48°F to 86°F) for up to 16 hours. Prior to administration, ensure the infusion solution comes to reach room temperature.

2. How Supplied/Storage and Handling Section
    a. The storage instructions lack clarity, which may lead to product storage errors. Therefore, we recommend the following revisions:

LUNSUMIO (mosunetuzumab-axgb) injection is a sterile, colorless, preservative-free solution supplied as follows:

- One 1 mg/mL single-dose vial in a carton (NDC 50242-159-01)
- One 30 mg/30 mL (1 mg/mL) single-dose vial in a carton (NDC 50242-142-01).

Store refrigerated at 2°C to 8°C (36°F to 46°F) in original carton to protect from light. Do not freeze. Do not shake.

4.2 RECOMMENDATIONS FOR GENENTECH, INC.

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

A. General Comments (Container labels & Carton Labeling)

1. As currently presented, the proprietary name is denoted by the placeholder "TRADENAME". Replace all presentations of the placeholder "TRADENAME" with the conditionally acceptable proprietary name, Lunsumio.
2. The Rx Only statement is prominent. The Rx Only statement appears prominent on the principal display panel. We recommend decreasing the prominence by debolding the Rx Only statement.
3. As currently presented, the format for the expiration date is not defined. We are unable to assess the proposed expiration date format from a medication safety perspective. To minimize confusion and reduce the risk for deteriorated drug medication errors, we recommend identifying the expiration date format you intend to use. FDA recommends that the human-readable expiration date on the drug package label include a year, month, and non-zero day. FDA recommends that the expiration date appear in YYYY-MM-DD format if only numerical characters are used or in YYYY-MMM-DD if alphabetical characters are used to represent the month. If there are space limitations on the drug package, the human-readable text may include only a year and month, to be expressed as: YYYY-MM if only numerical characters are used or YYYY-MMM if alphabetical characters are used to represent the month. FDA recommends that a hyphen or forward slash to separate the portions of the expiration date.

B. Carton Labeling

1. The storage information is not prominent on the side display panel. Lack of prominence of the storage information may result in product storage errors. On the side display panel, revise the storage information as follows, "Refrigerate at 2°C to 8°C (36°F to 46°F) in the original carton to protect from light. Do not freeze. Do not shake." We recommend this to increase the prominence of this important information and minimize the risk of the storage information being overlooked.

2. Add the net quantity statement “One 1 mL” and “One 30 mL” as a distinct item on the carton labeling in accordance with 21 CFR 201.51(a). To accommodate this change, consider revising to “One 1 mL vial” and “One 30 mL vial” on the principal display panel of the carton labeling.

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 2 presents relevant product information for Lunsumio received on April 29, 2022 from Genentech, Inc..

<table>
<tr><th colspan="2">Table 2. Relevant Product Information for Lunsumio</th></tr>
<tr><td>Initial Approval Date</td><td>N/A</td></tr>
<tr><td>Nonproprietary Name</td><td>mosunetuzumab-axgb</td></tr>
<tr><td>Indication</td><td>Indicated for the treatment of adult patients with relapsed or refractory follicular lymphoma who have received at least two prior systemic therapies.</td></tr>
<tr><td>Route of Administration</td><td>Intravenous infusion</td></tr>
<tr><td>Dosage Form</td><td>Injection</td></tr>
<tr><td>Strength</td><td>1 mg/mL, 30 mg/30 mL (1 mg/mL)</td></tr>
<tr><td>Dose and Frequency</td><td>
<table>
<tr><th colspan="2">Day of Treatment</th><th>Dose of LUNSUMIO</th><th>Rate of Infusion</th></tr>
<tr><td rowspan="3">Cycle 1</td><td>Day 1</td><td>1 mg</td><td rowspan="3">Administer over a minimum of 4 hours.</td></tr>
<tr><td>Day 8</td><td>2 mg</td></tr>
<tr><td>Day 15</td><td>60 mg</td></tr>
<tr><td>Cycle 2</td><td>Day 1</td><td>60 mg</td><td rowspan="2">Administer over 2 hours if infusions from cycle 1 were well-tolerated.</td></tr>
<tr><td>Cycles 3+</td><td>Day 1</td><td>30 mg</td></tr>
</table>
</td></tr>
<tr><td>How Supplied</td><td>Carton containing one 1 mg/1 mL single-dose vial (NDC 50242-159-01) or one 30 mg/30 mL single-dose vial (NDC 50242-142-01).</td></tr>
<tr><td>Storage</td><td>Store vials under refrigeration at 2°C to 8°C (36°F to 46°F) in original carton to protect from light. Do not freeze. Do not shake.</td></tr>
</table>

APPENDIX F. INFORMATION REQUEST

FDA Information Request: We acknowledge that you are proposing a peel-off sticker, “Do not use in-line filter”, that appears at the end of the Medication Guide and should be applied to the infusion bag prior to administration. Since the sticker is attached to the end of the Medication Guide, we request a 3D image of how the sticker will appear. For example, is the sticker visible right at the top of the insert or does someone have to open the insert to get to the sticker? Additionally, please provide your rationale for the peel-off sticker, the clinical consequence that may occur if an in-line filter is used during administration of the product, and if there were any administration errors observed during your clinical study using a filter.

Applicant Response received on September 6, 2022: See
\\CDSESUB1\EVSPROD\bla761263\0044\m1\us\20220906-response.pdf

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 Lunsumio labels and labeling submitted by Genentech, Inc..

- Container labels received on April 29, 2022
- Carton labeling received on April 29, 2022
- Peel-off sticker on the carton labeling insert received on September 6, 2022
- Prescribing Information and Medication Guide (Image not shown) received on August 10, 2022, available from \\CDSESUB1\EVSPROD\bla761263\0034\m1\us\draft-labeling-text.docx

G.2 Label and Labeling Images

Container labels

(b) (4)

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

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

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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/

NICOLE F IVERSON
09/12/2022 10:38:16 AM

HINA S MEHTA
09/12/2022 11:07:50 AM