CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761113Orig1s000

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:	January 14, 2020
To:	Kimberly Scott, RN, BSN, OCN Senior Regulatory Project Manager **Hematologic Malignancies 2** **Division of Regulatory Operations for Oncologic Diseases** **Office of Regulatory Operations**
Through:	LaShawn Griffiths, MSHS-PH, BSN, RN Associate Director for 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)** Adesola Adejuwon, PharmD, MBA Regulatory Review Officer **Office of Prescription Drug Promotion (OPDP)**
Subject:	Review of Patient Labeling: Patient Package Insert (PPI)
Drug Name (established name):	SARCLISA (isatuximab)
Dosage Form and Route:	injection, for intravenous use
Application Type/Number:	BLA 761113
Applicant:	Sanofi-Aventis U.S. LLC

1 INTRODUCTION

On April 30, 2019, Sanofi-Aventis U.S. LLC submitted for the Agency's review an original Biologics License Application (BLA) 761113 for SARCLISA (isatuximab) injection for the proposed indication: (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 Hematology Malignancies 2) on June 28, 2019, for DMPP and OPDP to review the Applicant's proposed Patient Package Insert (PPI) for SARCLISA (isatuximab) injection.

2 MATERIAL REVIEWED

- Draft SARCLISA (isatuximab) injection PPI received on April 30, 2019, and received by DMPP on December 31, 2019.
- Draft SARCLISA (isatuximab) injection Prescribing Information (PI) received on April 30, 2019, revised by the Review Division throughout the review cycle, and received by DMPP on January 8, 2019.
- Approved DARZALEX (daratumumab) injection labeling dated November 21, 2016 (S-004) and September 26, 2019 (S-024).

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, size 10.

In our collaborative review of the PPI we:

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

4 CONCLUSIONS

The PPI 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 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.

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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: January 14, 2020

To: Bindu Kanapuru, M.D., Clinical Reviewer
Division of Hematologic Malignancies 2 (DHM2)

Kimberly Scott, RN, BSN, OCN, Senior Regulatory Health Project Manager, DHM2

From: Adesola Adejuwon, Pharm D, MBA, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Kevin Wright, Pharm D, Team Leader, OPDP

Subject: OPDP Labeling Comments for SARCLISA® (isatuximab-irfc) injection, for intravenous use

BLA: 761113

In response to DHM2's consult request dated June 28, 2019, OPDP has reviewed the proposed product labeling (PI), patient package insert (PPI), and carton and container labeling for the original BLA submission for SARCLISA® (isatuximab-irfc) injection, for intravenous use.

PI and PPI: OPDP's comments on the proposed labeling are based on the draft PI received by electronic mail from DHM2 (Kimberly Scott) on January 8, 2020 and are provided below.

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

Carton and Container Labeling: OPDP has reviewed the attached proposed carton and container labeling submitted by the Sponsor to the electronic document room on November 15, 2019, and we do not have any comments.

Thank you for your consult. If you have any questions, please contact Adesola Adejuwon at (240) 402-5773 or Adesola.Adejuwon@fda.hhs.gov.

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MEMORANDUM

REVIEW OF REVISED LABEL AND LABELING
Division of Medication Error Prevention and Analysis (DMEPA)
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:	December 3, 2019
Requesting Office or Division:	Division of Hematologic Malignancies 2 (DHM 2)
Application Type and Number:	BLA 761113
Product Name and Strength:	Sarclisa (isatuximab-irfc) Injection, 100 mg/5 mL (20 mg/mL) and 500 mg/25 mL (20 mg/mL)
Applicant/Sponsor Name:	Sanofi Aventis US LLC
OSE RCM #:	2019-839-1
DMEPA Safety Evaluator:	Nicole Garrison, PharmD, BCPS
DMEPA Team Leader:	Hina Mehta, PharmD

1 PURPOSE OF MEMORANDUM

The Applicant submitted revised container labels and carton labeling received on November 26, 2019 for Sarclisa. We reviewed the revised container labels and carton labeling for Sarclisa (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 Applicant implemented all of our recommendations and we have no additional recommendations at this time.

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[a] Garrison N. Label and Labeling Review for Sarclisa (BLA 761113). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2019 NOV 05. RCM No.: 2019-839.

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LABEL AND LABELING REVIEW
Division of Medication Error Prevention and Analysis (DMEPA)
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:	November 5, 2019
Requesting Office or Division:	Division of Hematologic Malignancies 2 (DHM2)
Application Type and Number:	BLA 761113
Product Name and Strength:	Sarclisa (isatuximab-xxxx) Injection, 100 mg/5 mL (20 mg/mL) and 500 mg/ 25 mL (20 mg/mL)
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Sanofi Aventis US LLC
FDA Received Date:	April 30, 2019 and July 11, 2019
OSE RCM #:	2019-839
DMEPA Safety Evaluator:	Nicole Garrison, PharmD, BCPS
DMEPA Team Leader:	Hina Mehta, PharmD

1 REASON FOR REVIEW

As part of the approval process for BLA 761113 Sarclisa (isatuximab-xxxx) injection, 100 mg/5 mL (20 mg/mL) and 500 mg/ 25 mL (20 mg/mL), this review evaluates the proposed container labels, carton labeling, Patient Information, and Prescribing Information (PI) for areas 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 Label and Labeling 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

Sanofi Aventis US LLC submitted a 351 (a) application to obtain marketing approval of Sarclisa Injection (isatuximab-xxxx). Sarclisa is being proposed (b) (4)

We performed a risk assessment of the proposed container labels, carton labeling, Patient Information and Prescribing Information for Sarclisa (isatuximab-xxxx) Injection to determine whether there are significant concerns in terms of safety related to preventable medication errors. 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 recommend removing abbreviations and symbols, revising storage statements for clarity and revising the presentation of the nonproprietary name. For the Applicant, we recommend changes to the carton and container labels to improve readability and prominence of important information. Specifically, we recommend increasing prominence of the proprietary name, revising cautionary, net quantity, and storage statements on the labels and labeling. In addition we recommend defining the format of the expiration date on the container labels and including the NDC numbers.

4 CONCLUSION & RECOMMENDATIONS

We conclude that the proposed label and labeling can be improved to increase the readability and prominence of important information on the label to promote the safe use of the product. We provide recommendations below in Section 4.1 for the Division and Section 4.2 for Sanofi Aventis US LLC to address our concerns. We advise these recommendations are implemented prior to approval of this product.

4.1 RECOMMENDATIONS FOR THE DIVISION

A. Highlights of Prescribing Information

1. Dosage and Administration

   a. Relocate the third bullet with dose to second bullet and revise the statement, [redacted (b) (4)] to "The recommended dose of Sarclisa is 10 mg/kg as an intravenous infusion over 4 hours every week for 4 weeks followed by every 2 weeks in combination with pomalidomide and dexamethasone until disease progression or unacceptable toxicity."

   b. Revise [redacted (b) (4)] to "See Full Prescribing Information for instructions on preparation and administration. (2.4, 2.5)" for clarity as several steps are involved in preparation.

2. Dosage Forms and Strengths

   a. Revise to include the total concentration per vial and separate each strength into bullets for clarity. Revise to:

      - "Injection: 100 mg/5 mL (20 mg/mL) solution in single-dose vials (3)

- Injection: 500 mg/25 mL (20 mg/mL) solution in single-dose vials (3)

B. Prescribing Information

1. Dosage and Administration Section

   a. The dosage and administration section contains the abbreviations ("IV and "PO") and the symbol, "≥". We recommend avoiding the use of abbreviations and symbols in text that will be used to make dosing decisions. Replace abbreviations and symbols in relevant sections with the intended meanings.

   b. The non-standard abbreviation, "IR" is used in Section 2.5 *Administration* of the PI. Medication errors may result from the use of non-standard abbreviations; thus, we recommend replacing the abbreviation, "IR" with the intended meaning.

   c. Revise the third bullet in Section 2.4 to "Withdraw the necessary volume of Sarclisa and dilute by adding to the infusion bag containing 250 mL of 0.9% Sodium Chloride Injection, USP or 5% Dextrose Injection."

   d. Remove the fourth bullet in Section 2.5 which states (b) (4)

2. Dosage Forms and Strengths

   a. Include the total concentration per total volume to prevent confusion. We recommend including "100 mg/5 mL (20 mg/mL)" and "500 mg/25 mL (20 mg/mL)".

3. How Supplied/Storage and Handling Section

   a. Revise the storage statements as follows, "Store refrigerated at 36°F to 46°F (2°C to 8°C) in the original carton to protect from light. Do not freeze. Do not shake." We recommend this revision to be consistent with the carton labeling.

   b. As currently presented, the NDC number is denoted by a placeholder (0000-000-00). We request that you submit the NDC numbers for the Prescribing Information.

C. Patient Information

1. Revise the presentation of the nonproprietary from "isatuximab" to "isatuximab-xxxx". We recommend this revision to be consistent with the PI, container labels, and carton labeling.

4.2 RECOMMENDATIONS FOR SANOFI AVENTIS US LLC

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

A. General Comments (Container labels & Carton Labeling)

1. Include the dosage form "Injection" to appear below the proper name as follows:

   Sarclisa
   (isatuximab-xxxx)
   Injection

   Revise the font color of the proprietary name ((b) (4) color) or revise the font color of the 100 mg/5 mL strength ((b) (4) color) and 500 mg/25 mL ((b) (4) color), so that either the strength or the proprietary name appears in its own unique color and the color does not overlap with any other colors utilized in highlighting the strengths. The use of the same (b) (4) color font for the proprietary name and the product's strengths minimizes the difference between the strengths, which may lead to wrong strength selection errors.
2. Revise the statement, (b) (4) to "For Intravenous Infusion After Dilution." We recommend this to minimize the risk of the product being administered without dilution.
3. As currently presented, the NDC number is denoted by a placeholder (0000-000-00). We request that you submit the NDC numbers for the container labels and carton labeling.
4. 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 be used to separate the portions of the expiration date.

B. Container Labels

1. Revise the statement, [redacted]
2. Revise the statement, [redacted]
3. If space permits, revise the storage statement, [redacted]

A. Carton Labeling

1. Decrease the prominence of the net quantity statement by debolding the statement to appear as [redacted] and revise the statement to appear as “One single-dose vial”.
2. Revise the statement, [redacted] to “Dosage: See Prescribing Information.”
3. Delete the statement, [redacted] as reference is made to the Prescribing Information on the rear display panel .”
4. Revise the storage statements, [redacted] to “Store refrigerated at 36°F-46°F (2°C-8°C) in the carton to protect from light. Do not freeze. Do not shake.”
5. Consider relocating the expression of strength on the side panels and place above the route of administration statement.

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 2 presents relevant product information for Sarclisa received on July 11, 2019 from Sanofi Aventis US LLC.

Table 2. Relevant Product Information for Sarclisa	
Initial Approval Date	N/A
Active Ingredient	isatuximab-xxxx
Indication	(b) (4)
Route of Administration	Intravenous infusion
Dosage Form	Injection
Strength	100 mg/5 mL (20 mg/mL) and 500 mg/ 25 mL (20 mg/mL)
Dose and Frequency	10 mg/kg body intravenously every week for 4 weeks followed by every 2 weeks until disease progression or unacceptable toxicity.
How Supplied	• 100 mg/5 mL single dose vial in a carton • 500 mg/25 mL single-dose vial in a carton
Storage	(b) (4) Do not Freeze. Do not shake. (b) (4)

APPENDIX B. PREVIOUS DMEPA REVIEWS

On August 22, 2019, we searched for previous DMEPA reviews relevant to this current review using the terms, Sarclisa. Our search did not identify any 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,[a] along with postmarket medication error data, we reviewed the following Sarclisa labels and labeling submitted by Sanofi Aventis US LLC.

- Container labels received on April 30, 2019
- Carton labeling received on April 30, 2019
- Prescribing Information (Image not shown) received on July 11, 2019

G.2 Label and Labeling Images

(b) (4)

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

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CLINICAL INSPECTION SUMMARY

Date	November 4, 2019
From	Anthony Orencia M.D., F.A.C.P., Medical Officer Min Lu, M.D., M.P.H., Team Leader Kassa Ayalew, M.D., M.P.H., Branch Chief Good Clinical Practice Assessment Branch Division of Clinical Compliance Evaluation Office of Scientific Investigations
To	Bindu Kanapuru, M.D., Medical Officer Nicole Gormley, M.D., Team Leader Ann Farrell, M.D., Director Saumya Nathan, Project Manager Division of Hematology Products
BLA	761113
Applicant	Sanofi US Services Inc., on behalf of Sanofi-Aventis U.S. LLC, A Sanofi Company
Drug	Isatuximab (SAR650984)
NME	Yes
Division Classification	Chimeric monoclonal antibody with anti-CD38 activity
Proposed Indication	Combination treatment with pomalidomide and dexamethasone for patients with relapsed/refractory multiple myeloma
Consultation Request Date	July 1, 2019
Summary Goal Date	November 30, 2019
Action Goal Date	February 28, 2020
PDUFA Date	February 28, 2020

I. OVERALL ASSESSMENT OF FINDINGS AND RECOMMENDATIONS

Two clinical investigator sites (Drs. Ivan Spicka and Xavier Leleu) were selected for inspection for Study EFC14335 in BLA 761113.

Based on the results of the inspections, the study data derived from these clinical investigator sites are considered reliable, and the study in support of this application appears to have been conducted adequately.

II. BACKGROUND

Isatuximab (SAR650984) is a chimeric monoclonal antibody (mAb) that binds selectively to an epitope on the human surface antigen CD38. Isatuximab kills tumor cells via multiple biological mechanisms, including antibody-dependent cellular-mediated cytotoxicity (ADCC), complement-dependent cytotoxicity (CDC), direct induction of apoptosis without crosslinking, and inhibition of CD38 enzymatic activity. Its anti-CD38 activity is proposed by sponsor as a potential combination treatment with pomalidomide and dexamethasone for patients with relapsed/refractory multiple myeloma, who were previously treated with at least two lines of therapy.

A single study, EFC14335, will form the basis for the regulatory decision-making process for this application. The Division of Hematology Products (DHP) requests inspection of two international clinical sites, due to inadequate domestic site data to support their application.

Study EFC14335

Study EFC14335 was a Phase 3, multicenter, multinational, randomized, open-label, parallel group, two-arm study evaluating the efficacy of isatuximab in combination with pomalidomide and dexamethasone (IPd) compared with pomalidomide and dexamethasone (Pd) for the treatment of patients with refractory or relapsed and refractory multiple myeloma (MM) who had received at least two prior lines of therapy including lenalidomide and a proteasome inhibitor (bortezomib, carfilzomib or ixazomib) alone or in combination, and have demonstrated disease progression on or within 60 days of completion of the last therapy.

The primary objective was to demonstrate the benefit of IPd in the prolongation of progression-free survival (PFS) as compared to Pd in patients with refractory or relapsed and refractory multiple myeloma.

The primary efficacy endpoint was comparison of progression free survival, as assessed by an Independent Review Committee, in the IPd group versus the Pd group stratified by age and number of previous lines of therapy. The cut-off date for the analysis of PFS was the actual date when the162 events (first occurrence of either disease progression or death due to any cause) were observed. The secondary efficacy endpoint comprised overall survival and overall treatment response “rate” (ORR).

The study was conducted in 24 countries. A total of 307 subjects were randomized, and 301 patients were treated. The first study patient was enrolled on January 10, 2017. The date of last recorded patient visit was November 22, 2018. This study is ongoing.

III. RESULTS (by site):

1. Ivan Spicka, M.D., Ph.D., Site #2030003
I. interni klinika - klinika hematologie
U Nemocnice 499/2
Prague 28, 128 00
Czech Republic

Inspection dates: September 24 to 27, 2019

A total of ten subjects were screened and enrolled. Ten study subjects received treatment in the randomized portion of the study. Seven patients discontinued due to disease progression and two study subjects withdrew from the study due to serious adverse events. An audit was conducted for all enrolled subjects.

Source documents were verified against the case report forms and BLA subject line listings for study eligibility, informed consent form, IRB review/approval, monitoring, test article accountability, concomitant medication, delegation of authority, primary and secondary efficacy endpoint, and adverse event/serious adverse event reporting. Records review of the enrolled subjects indicated that the eligibility criteria for enrollment were met.

Source documents for the raw data used to assess the primary efficacy endpoint were verifiable at the study site. All primary and secondary endpoint data was verified using site data and confirmed with the data from the central adjudication committee provided by the sponsor representatives at the inspection. The data at the site matched the data from the adjudication committee and the data line listings.

There was no under-reporting of adverse events. There were no limitations during conduct of the clinical site inspection.

In general, this clinical site appeared to be in compliance with Good Clinical Practice. A Form FDA 483 (Inspectional Observations) was not issued at the end of the inspection.

2. Xavier Leleu, M.D., Ph.D., Site #2500007
Oncologie hématologique
2 rue de la Milétrie
Poitiers, 86000
France

Inspection dates: September 18 to 20, 2019

A total of ten subjects were screened, and nine patients enrolled. Nine enrolled patients received treatment in the randomized portion of the study. Seven study subjects discontinued further treatment from the study due to disease progression.

For this inspection, a complete review of regulatory documentation at the study site was performed. Source records for the ten subjects screened at the site were reviewed. The records reviewed included medical records, regulatory binder documents, delegation logs and signature logs, training logs, source data worksheets, informed consent forms, monitoring follow-up reports, and pharmacy records.

Source documents for all enrolled subjects were verified against the case report forms and BLA subject line listings for eligibility, adverse events, and serious adverse event reporting. Source documents for the primary and secondary efficacy endpoint raw data were verifiable at the study site. There was no under-reporting of adverse events.

There were no limitations during conduct of the clinical site inspection.

In general, this clinical site appeared to be in compliance with Good Clinical Practice. A Form FDA 483 (Inspectional Observations) was not issued at the end of the inspection.

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

CONCURRENCE:

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Kassa Ayalew, M.D., M.P.H.
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Division of Hematology Products Associate Director for Labeling Review of the Prescribing Information

Product Title	**SARCLISA™ (isatuximab-xxxx) injection, for intravenous use**
Applicant	sanofi-aventis U.S. LLC
Application/Supplement Number	BLA 761113
Type of Application/Submission[1]	Original BLA
Is Proposed Labeling in Old Format? (Y/N)	N
Is Labeling Being Converted to PLR? (Y/N)	N
Is Labeling Being Converted to PLLR? (Y/N)	N
Proposed Indication(s) (if applicable)	(b) (4) [redacted]
Approved Indication(s) (if applicable)	n/a
Date FDA Received Application	4/30/19
Review Classification (Priority/Standard)	Priority
Action Goal Date	10/30/19
Review Date	07/11/19
Reviewer	Virginia Kwitkowski, MS, ACNP-BC

This Associate Director for Labeling (ADL) review provides recommendations on the content and format of the prescribing information (PI) to help ensure that PI:

- Is compliant with Physician Labeling Rule (PLR) and Pregnancy and Lactation Labeling Rule (PLLR) requirements[2]
- Is consistent with labeling guidance recommendations[3] and with CDER/OND best labeling practices and policies
- Conveys the essential scientific information needed for safe and effective use of the product
- Is clinically meaningful and scientifically accurate
- Is a useful communication tool for health care providers
- Is consistent with other PI with the same active moiety, drug class, or similar indication

The applicant is seeking approval of their original BLA for isatuximab (b) (4) [redacted]

[1] Examples include: Original Biologics License Application (BLA), New Molecular Entity (NME) NDA, Original NDA, NDA Efficacy Supplement, 505(b)(2) New Drug Application (NDA), New Chemical Entity (NCE) NDA, NDA Prior Approval Labeling Supplement, NDA CBE-0 Labeling Supplement

[2] See *January 2006 Physician Labeling Rule*; 21 CFR 201.56 and 201.57; and *December 2014 Pregnancy and Lactation Labeling Rule* (the PLLR amended the PLR regulations). For applications with labeling in non-PLR "old" format, see 21 CFR 201.56(e) and 201.80.

[3] See *PLR Requirements for PI* website for PLR labeling guidances.

This review is being completed before mid-cycle.

In the attached PI, ADL comments (in balloons) begin with my name.

During my review, I considered the currently approved Darzalex labeling, given that they share an established pharmaceutical class as well as indication (multiple myeloma).

ADL recommendations provided in this review (e.g., recommended edits and comments regarding parts of PI) are preliminary and pending discussion with other review team members for this product.

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