Our STN: BL 125736/218

SUPPLEMENT APPROVAL
April 4, 2024

Celgene Corporation, a Bristol-Myers Squibb Company
Attention: Brittany Dustman, PharmD, MS, RAC
Director, Global Regulatory Strategy and Policy
3401 Princeton Pike
Lawrenceville, NJ 08648

Dear Dr. Dustman:

We have approved your request received February 15, 2023, to supplement your Biologics License Application (BLA) submitted under section 351(a) of the Public Health Service Act for idecabtagene vicleucel to include an indication for the treatment of adult patients with relapsed or refractory multiple myeloma after two or more prior lines of therapy including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody.

We have also approved a major modification to the approved Risk Evaluation and Mitigation Strategy (REMS) to minimize the burden on the healthcare delivery system of complying with the REMS.

The review of this supplement was associated with the following National Clinical Trial (NCT) numbers: NCT03361748; NCT03601078; NCT03651128; NCT03435796; and NCT02658929.

LABELING

Under 21 CFR 201.57(c)(18), patient labeling must be referenced in section 17 PATIENT COUNSELING INFORMATION. Patient labeling must be available and may either be reprinted immediately following the full prescribing information of the package insert or accompany the prescription product labeling.

We hereby approve the draft content of labeling Package Insert submitted under amendment 65, dated April 4, 2024, and Medication Guide submitted under amendment 65, dated April 4, 2024, and the draft carton and container labels submitted under amendment 0, dated February 15, 2023.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the final content of labeling (21 CFR 601.14) in Structured Product Labeling (SPL)

format via the FDA automated drug registration and listing system, (eLIST) as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the Package Insert and Medication Guide submitted on April 4, 2024. Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As* at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.
The SPL will be accessible via publicly available labeling repositories.

We request that the labeling approved today be available on your website within 10 days of receipt of this letter.

CARTON AND CONTAINER LABELS

Please electronically submit final printed carton and container labels identical to the carton and container labels submitted on [DATE], according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications* at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/providing-regulatory-submissions-electronic-format-certain-human-pharmaceutical-product-applications.

All final labeling should be submitted as Product Correspondence to this BLA, STN BL 125736 at the time of use and include implementation information on Form FDA 356h.

ADVERTISING AND PROMOTIONAL LABELING

You may submit two draft copies of the proposed introductory advertising and promotional labeling with Form FDA 2253 to the Advertising and Promotional Labeling Branch at the following address:

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
10903 New Hampshire Ave.
WO71–G112
Silver Spring, MD 20993-0002

You must submit copies of your final advertising and promotional labeling at the time of initial dissemination or publication, accompanied by Form FDA 2253 (21 CFR 601.12(f)(4)).

All promotional claims must be consistent with and not contrary to approved labeling. You should not make a comparative promotional claim or claim of superiority over other

products unless you have substantial evidence or substantial clinical experience to support such claims (21 CFR 202.1(e)(6)).

For each pending supplemental application for this BLA that includes proposed revised labeling, please submit an amendment to update the proposed revised labeling with the change[s] approved today.

PEDIATRIC REQUIREMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because the biological product for this indication has an orphan drug designation, you are exempt from this requirement.

RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENTS

The REMS for idecabtagene vicleucel (ABECMA) was originally approved on March 26, 2021, and the most recent REMS modification was approved on April 20, 2021. The REMS consists of elements to assure safe use, an implementation system, and a timetable for submission of assessments of the REMS.

In accordance with section 505-1(g)(4)(B) of the Federal Food, Drug, and Cosmetic Act (FDCA), we have determined that your approved REMS for ABECMA must be modified to minimize the burden on the healthcare delivery system of complying with the REMS. Your approved REMS must be modified as follows:

- Modification to REMS goals: The goal for “Ensuring that those who prescribe, dispense, or administer ABECMA are aware of how to manage the risks of CRS and neurologic toxicities” is no longer necessary to ensure the benefits of the drug outweigh the risks and must be removed.
- Removal of requirement for educational and training materials: Patient Wallet Card, Training Program, Knowledge Assessment, and Adverse Reaction Management Guide.
- Removal of requirement to report any serious adverse events suggestive of CRS or neurologic toxicities to the REMS Program.

Your proposed modified REMS submitted April 2, 2024, and appended to this letter, is approved.

The timetable for submission of assessments of the REMS remains the same as that approved on March 26, 2021. The REMS assessment plan has been revised to remove education statistics to align with the above REMS modification. The REMS assessment plan must include, but is not limited to, the following:

For annual assessments:

The REMS Program Infrastructure and Performance (provide in tabular format as appropriate):

A. Hospitals and their associated clinics enrollment (provide for each reporting period and cumulatively)
    - List of all ABECMA REMS Certified Care Centers. Include locations, dates of enrollment, and method of enrollment and dates of certification notification;
    - Number of incomplete enrollments at the time of assessment data lock.

B. Utilization of ABECMA
    - Number of ABECMA shipments sent to Certified Care Centers (current reporting period and cumulative), stratified by Certified Care Center type.
    - Number of unique patients treated with ABECMA at each Certified Care Center; Include the following demographics if available: age;
    - Number and age of patients for which ABECMA was ordered but never infused and the reason(s) that the patient was not treated; provide number of occurrences at each Certified Care Center for each reporting period and cumulatively;
    - Time between certification and first order for ABECMA for each Certified Care Center during the assessment period.

C. Compliance with ABECMA REMS
    - Number and name of non-certified hospital(s) that have treated a patient with ABECMA and any corrective actions taken to prevent future occurrences and the number of these that subsequently became certified (current reporting period and cumulative)
    - Audits: A summary of findings from first-order audits and annual audits (current reporting period) by type of audit deficiencies and stratified by type of center (i.e., clinic or hospital)
    - Summary report of all non-compliance, associated corrective and preventative actions (CAPA), and the status of CAPA plans.

D. ABECMA REMS Customer Care Center
    - Number of calls received by stakeholder type (patient/guardian, prescriber, hospital and their associated clinic authorized

representative, other health care provider [HCP], other) and reason for the call;
- Summary of frequently asked questions (FAQ) by stakeholder type;
- A description of each call, including stakeholder type, that may indicate an issue with product access due to the REMS program, REMS program burden, or an adverse event;
- A summary of corrective or preventive actions resulting from issues identified;
- Summary of any non-compliance that is identified through call center contacts, source of report and resulting corrective and preventative actions.

E. With respect to each goal included in the strategy, an assessment of the extent to which the approved strategy, including each element of the strategy, is meeting the goal or whether one or more such goals or such elements should be modified (Section 505-1(g)(3)).

The requirements for assessments of an approved REMS under section 505-1(g)(3) include with respect to each goal included in the strategy, an assessment of the extent to which the approved strategy, including each element of the strategy, is meeting the goal or whether 1 or more such goals or such elements should be modified.

We remind you that in addition to the REMS assessments submitted according to the timetable in the approved REMS, you must include an adequate rationale to support any proposed REMS modification for the addition, modification, or removal of any goal or element of the REMS, as described in section 505-1(g)(4) of the FDCA.

We also remind you that you must submit a REMS assessment when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of the FDCA. This assessment should include:

a) An evaluation of how the benefit-risk profile will or will not change with the new indication;
b) A determination of the implications of a change in the benefit-risk profile for the current REMS;
c) *If the new indication for use introduces unexpected risks*: A description of those risks and an evaluation of whether those risks can be appropriately managed with the currently approved REMS.
d) *If a REMS assessment was submitted in the 18 months prior to submission of the supplemental application for a new indication for use*: A statement about whether the REMS was meeting its goals at the time of the last assessment and if any modifications of the REMS have been proposed since that assessment.
e) *If a REMS assessment has not been submitted in the 18 months prior to submission of the supplemental application for a new indication for use*: Provision of as many of the currently listed assessment plan items as is feasible.

f) *If you propose a REMS modification based on a change in the benefit-risk profile or because of the new indication of use, submit an adequate rationale to support the modification, including*: Provision of the reason(s) why the proposed REMS modification is necessary, the potential effect on the serious risk(s) for which the REMS was required, on patient access to the drug, and/or on the burden on the health care delivery system; and other appropriate evidence or data to support the proposed change. Additionally, include any changes to the assessment plan necessary to assess the proposed modified REMS.
g) *If you are not proposing REMS modifications*, provide a rationale for why the REMS does not need to be modified.

If the assessment instruments and methodology for your REMS assessments are not included in the REMS supporting document, or if you propose changes to the submitted assessment instruments or methodology, you should update the REMS supporting document to include specific assessment instrument and methodology information at least 90 days before the assessments will be conducted. Updates to the REMS supporting document may be included in a new document that references previous REMS supporting document submission(s) for unchanged portions. Alternatively, updates may be made by modifying the complete previous REMS supporting document, with all changes marked and highlighted. Prominently identify the submission containing the assessment instruments and methodology with the following wording in bold capital letters at the top of the first page of the submission:

BLA 125736 REMS CORRESPONDENCE
(insert concise description of content in bold capital letters, e.g., **UPDATE TO REMS SUPPORTING DOCUMENT – ASSESSMENT METHODOLOGY**)

Prominently identify any submission containing the REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

BLA 125736 REMS ASSESSMENT

or

NEW SUPPLEMENT FOR BLA 125736
CHANGES BEING EFFECTED IN 30 DAYS
PROPOSED MINOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR BLA 125736
PRIOR APPROVAL SUPPLEMENT
PROPOSED MAJOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR BLA 125736
PRIOR APPROVAL SUPPLEMENT
PROPOSED REMS MODIFICATIONS DUE TO SAFETY LABEL CHANGES
SUBMITTED IN SUPPLEMENT [125736/####]

or

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR BLA 125736 REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

Should you choose to submit a REMS revision, prominently identify the submission containing the REMS revisions with the following wording in bold capital letters at the top of the first page of the submission:

REMS REVISION FOR BLA 125736

To facilitate review of your submission, we request that you submit your proposed modified REMS and other REMS-related materials in Microsoft Word format. If certain documents, such as enrollment forms, are only in PDF format, they may be submitted as such, but the preference is to include as many as possible in Word format.

SUBMISSION OF REMS DOCUMENT IN SPL FORMAT

As soon as possible, but no later than 14 days from the date of this letter, submit the REMS document in Structured Product Labeling (SPL) format using the FDA automated drug registration and listing system (eLIST). Content of the REMS document must be identical to the approved REMS document. The SPL will be publicly available.

Information on submitting REMS in SPL format may be found in the guidance for industry *Providing Regulatory Submission in Electronic Format – Content of the Risk Evaluation and Mitigation Strategies Document Using Structured Product Labeling*.

For additional information on submitting REMS in SPL format, please email FDAREMSwebsite@fda.hhs.gov.

We remind you that you must comply with reporting requirements for an approved BLA (in 21 CFR 600.80 and in 21 CFR 600.81).

We will include information contained in the above-referenced supplement in your BLA file.

Sincerely,

Lola Fashoyin-Aje, MD, MPH
Acting Director
Division of Clinical Evaluation Hematology
Office of Clinical Evaluation
Office of Therapeutic Products
Center for Biologics Evaluation and Research

Enclosures:
REMS