Our STN: BL 125643/530

NOTIFICATION
SAFETY LABELING CHANGE
January 19, 2024

Kite Pharma, Inc.
Attention: Arjana Pradhan
2400 Broadway
Santa Monica, CA 90404

Dear Dr. Pradhan:

Please refer to your Biologics License Application (BLA) submitted under section 351(a) of the Public Health Service Act for axicabtagene ciloleucel.

Section 505(o)(4) of the Federal Food, Drug, and Cosmetic Act (FDCA) authorizes FDA to require holders of approved drug and licensed biological product applications to make safety related labeling changes based upon new safety information that becomes available after approval of the drug or biological product.

Since YESCARTA (axicabtagene ciloleucel) was approved on October 18, 2017, we have become aware of the risk of T cell malignancies, with serious outcomes, including hospitalization and death, following treatment with BCMA- and CD19-directed genetically modified autologous T cell immunotherapies. FDA identified postmarketing adverse event and clinical trial reports describing occurrence of mature T cell malignancies, including CAR-positive tumors, following treatment with BCMA- and CD19-directed genetically modified autologous T cell immunotherapies. For additional information please see CBER safety communication titled, "*FDA Investigating Serious Risk of T-cell Malignancy Following BCMA-Directed or CD19-Directed Autologous Chimeric Antigen Receptor (CAR) T cell Immunotherapies*," and a posting at *July - September 2023 | Potential Signals of Serious Risks/New Safety Information Identified by the FDA Adverse Event Reporting System (FAERS) | FDA* for BCMA- or CD19-directed genetically modified autologous T cell immunotherapies. We consider this information to be "new safety information" as defined in section 505-1(b)(3) of the FDCA. Furthermore, we consider the serious risk of T cell malignancy to be applicable to all BCMA- and CD19-directed genetically modified autologous T cell immunotherapies.

In accordance with section 505(o)(4) of the FDCA, we are notifying you that based on the new safety information described above and discussed during the January 19, 2024 teleconference, we determined that the new safety information should be included in the labeling for all BCMA- and CD19-directed genetically modified autologous T cell immunotherapies. For YESCARTA (axicabtagene ciloleucel), we

have determined that the new safety information should be included in the labeling as follows:

1. **Boxed Warning, Highlights Section of the Prescribing Information (PI)**
   T cell malignancies have occurred following treatment with BCMA- and CD19-directed genetically modified autologous T cell immunotherapies, including YESCARTA. (5.8)

2. **Boxed Warning, Full Prescribing Information**
   T cell malignancies have occurred following treatment with BCMA- and CD19-directed genetically modified autologous T cell immunotherapies, including YESCARTA [see WARNINGS AND PRECAUTIONS (5.8)].

3. **WARNINGS AND PRECAUTIONS, Secondary Malignancies, Highlights Section of the PI**
   Secondary malignancies: T cell malignancies have occurred following treatment with BCMA- and CD19-directed genetically modified autologous T cell immunotherapies, including YESCARTA. (5.8)

4. **WARNINGS AND PRECAUTIONS, 5.8 Secondary Malignancies, Full Prescribing Information**
   T cell malignancies have occurred following treatment with BCMA- and CD19-directed genetically modified autologous T cell immunotherapies, including YESCARTA. Mature T cell malignancies, including CAR-positive tumors, may present as soon as weeks following infusion, and may include fatal outcomes. [See BOXED WARNING, ADVERSE REACTIONS (6.3), PATIENT COUNSELING INFORMATION (17).]

5. **ADVERSE REACTIONS, 6.3 Postmarketing Experience**
   Because adverse events to marketed products are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to product exposure.

   The following adverse event has been identified during postmarketing use of YESCARTA.

   Neoplasms: T cell malignancies

6. **Section 17 PATIENT COUNSELING INFORMATION**
   Secondary Malignancies
   Secondary malignancies, including T cell malignancies, have occurred [*see BOXED WARNING, WARNINGS AND PRECAUTIONS (5.8), ADVERSE REACTIONS (6.3)*].

7. **MEDICATION GUIDE**
   YESCARTA can increase your risk of getting cancers including certain types of cancers of the immune system. Your provider should monitor you for this.

In accordance with section 505(o)(4), within 30 calendar days of the date of this letter, you must submit a supplement proposing changes to the approved labeling in accordance with the above direction or notify FDA that you do not believe a labeling change is warranted and submit a rebuttal statement detailing the reasons why such a change is not warranted. If you submit a supplement that includes only language identical to that specified above, the supplement may be submitted as a changes being effected (CBE-0) supplement. If the supplement includes proposed language that differs from that above, submit a prior approval supplement (PAS).

Under section 505(o)(4), if you fail to submit a response within 30 calendar days, you would be in violation of the FDCA that may deem your product to be misbranded under section 502(z) and may subject you to enforcement action, including civil monetary penalties under section 303(f)(4)(A) and an order to make whatever labeling changes FDA deems appropriate to address the new safety information.

Please submit your safety labeling submission to STN 125643.

Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate:

SAFETY LABELING CHANGES UNDER 505(o)(4) - PRIOR APPROVAL SUPPLEMENT

OR

SAFETY LABELING CHANGES UNDER 505(o)(4) – CHANGES BEING EFFECTED

OR

SAFETY LABELING CHANGES UNDER 505(o)(4) – REBUTTAL (CHANGE NOT WARRANTED)."

Prominently identify subsequent submissions related to the safety labeling changes supplement with the following wording in bold capital letters at the top of the first page of the submission:

SAFETY LABELING CHANGES UNDER 505(o)(4) - AMENDMENT

If you have any questions, please contact the Regulatory Project Manager, Nevitt Morris, at (240) 402-8269 or by email at Nevitt.Morris@fda.hhs.gov.

Sincerely,

Nicole Verdun, MD
Director
Office of Therapeutic Products
Center for Biologics Evaluation and Research