From: Cagungun, Nannette
Sent: Wednesday, July 19, 2017 5:34 PM
To: 'Manisha.patel@novartis.com'
Cc: Giordano, Erica
Subject: Information Request

Our Reference: BL 125646/0

Dear Ms. Patel:

I am writing on behalf of Ms. Erica Giordano.

After reviewing the safety and CMC data for KYMRIAH, we have determined that there is potential for the serious risk of secondary malignancy due to replication-competent retrovirus or insertional mutagenesis. Therefore, a Post Marketing Requirement (PMR) based on section 505(o)(3)(B)(iii) of FDAAA: “to identify unexpected serious risk(s) when available data indicate the potential for serious risk(s)” is necessary.

The PMR should consist of a Phase IV, multi-center, prospective, observational, non-interventional, post market study. The primary objective of this study should be to characterize the type, frequency, and severity of all secondary malignancies in patients who receive KYMRIAH and it should enroll at least 1,000 patients and follow them for 15 years. Cases of relapse of the primary malignancy (B cell precursor acute lymphoblastic leukemia [ALL]) would be included as secondary malignancies. Fresh tumor tissue should be obtained and sent to Novartis to analyze for persistence of KYMRIAH as described in Protocol B2401 for secondary malignancies and relapsed ALL. Additional vector integration analyses may be needed depending on the results of the product persistence analyses.

We have reviewed the registry protocol that was submitted (CTL019 B2401), and find it acceptable, except for the changes outlined above.

Please submit a revised protocol for this PMR with the following milestone dates: Final Protocol Submission, Study Completion, and Final Report Submission.

Please submit your response to this information request as an amendment to this file by July 28, 2017 referencing the date of this request. If you anticipate you will not be able to respond by this date, please contact the Agency immediately so a new response date can be identified.

If you have any questions, please contact Ms. Giordano at (240) 402-8298 or erica.giordano@fda.hhs.gov.

Sincerely,
Nannette Cagungun, MS, PD, RAC
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