Abecma, Breyanzi, Carvykti, Kymriah, Tecartus and Yescarta (CD19- or BCMA-directed CAR T-cell therapies): Risk of secondary malignancy of T-cell origin

Dear Healthcare professional,

<Bristol-Myers Squibb Pharma EEIG, Janssen-Cilag International NV, Kite Pharma EU B.V. and Novartis Europharm Limited>, in agreement with the European Medicines Agency and the <National Competent Authority>, would like to inform you of the following:

Summary

- **Secondary malignancies of T-cell origin, including chimeric antigen receptor (CAR)-positive malignancies, have been reported within weeks and up to several years following treatment of haematological malignancies with a BCMA- or CD19-directed CAR T-cell therapy.**
- **Patients should be monitored life-long for secondary malignancies.**

Background on the safety concern

Currently approved CD19- or BCMA-directed CAR-T cell therapies cover a range of indications spanning from B-cell acute leukaemia, specific subtypes of B-cell lymphoma, and multiple myeloma.

Up to April 2024, approximately 42,500 patients have been treated with these medicinal products globally.

The European Medicines Agency (EMA) has evaluated 38 cases of T-cell malignancy that have been reported to occur after treatment with CAR T-cell therapies up to April 2024. These cases related to different types of T-cell lymphoma and of T-cell lymphocytic leukaemia and were observed within weeks and up to several years after administration. There have been fatal outcomes.

Among the cases included in this review, further testing regarding the presence of the CAR-construct in the secondary malignancy had been undertaken for less than half of the reported T-cell malignancies. In 7 cases, the CAR-construct was detectable. This suggests that the CAR T-cell therapy was involved in disease development and insertional mutagenesis could have occurred. While other mechanisms may also be possible, further investigation is desirable to better understand and identify underlying mechanisms and contributing factors. Therefore, testing of T-cell malignancy tissue samples from patients is one important step for such investigations.

Since approval, the product information has advised that patients treated with these products may develop secondary malignancies. The product information will be updated to include the new information concerning secondary malignancy of T-cell origin. Patients treated with CAR T-cell products should be monitored life-long for secondary malignancies.

Call for reporting

Healthcare professionals should report any suspected adverse reactions associated with the use of CAR T-cell products in accordance with the national spontaneous reporting system <*include the details (e.g. name, postal address, fax number, web address) on how to access the national spontaneous reporting system*>.

Please report the product name and batch details.

These medicinal products are subject to additional monitoring.