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(來函請敍明此檔案號碼) DH DO DIMC/7-30/1
(IN REPLY PLEASE QUOTE THIS FILE REF.)

24 Jan 2024

Dear Healthcare Professionals,

BCMA- and CD19-directed genetically modified autologous chimeric antigen receptor (CAR) T cell immunotherapies: risk of T cell malignancies

Your attention is drawn to the United States Food and Drug Administration's (FDA) announcement that the FDA issued safety labeling change notification letters to all manufacturers of licensed BCMA- and CD19-directed genetically modified autologous chimeric antigen receptor (CAR) T cell immunotherapies (Abecma, Breyanzi, Carvykti, Kymriah, Tecartus, Yescarta) requiring a revision to the package insert due to risk of T cell malignancies, with serious outcomes, including hospitalization and death.

The FDA considers the serious risk of T cell malignancy to be applicable to all BCMA- and CD19-directed genetically modified autologous T cell immunotherapies. The letters notify manufacturers of each such licensed product to update the package insert to include available information related to the risks and to update the Medication Guide for these products to identify the possibility of the increased risk of getting cancers, including certain types of cancers of the immune system.

In Nov 2023, the FDA posted a safety communication to provide information related to the receipt of reports of T cell malignancies, including CAR-positive lymphoma, in patients who received treatment with BCMA- or CD19-directed autologous CAR T cell immunotherapies. Reports were received from clinical trials and/or postmarketing adverse event data sources. Although the overall benefits of these products continue to outweigh their potential risks for their approved uses, the FDA continues to investigate the identified risk of T cell malignancy with serious outcomes, including hospitalization and death.

Patients and clinical trial participants receiving treatment with these products should be monitored life-long for new malignancies. In the event that a new malignancy occurs following treatment with these products, clinicians are encouraged to contact the manufacturer to report the event and obtain

instructions on collection of patient samples for testing for the presence of the CAR transgene.

Please refer to the following website in FDA for details:
https://www.fda.gov/news-events/press-announcements/fda-roundup-january-23-2024

In Hong Kong, Kymriah (tisagenlecleucel) Dispersion For Infusion (HK-66588) is a pharmaceutical product registered by Novartis Pharmaceuticals (HK) Limited. It is a prescription-only medicine. So far, with regard to tisagenlecleucel, the Department of Health (DH) has received 18 cases of adverse drug reaction, of which 8 cases were reported as malignancies. The other products mentioned in the above FDA's announcement are not registered pharmaceutical products.

Related news was previously issued by FDA and European Medicines Agency, and was posted on the Drug Office website on 29 Nov 2023 and 15 Jan 2024.

In light of the above FDA's announcement, the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

Please note that this letter serves as a means for the DH to communicate important new safety information about registered pharmaceutical products with healthcare professionals in Hong Kong and is not intended to serve as guidelines or to replace professional clinical judgement. Healthcare professionals are advised to balance the risk of possible adverse effects against the benefit of treatment.

Please report any adverse events caused by drugs to the Clinical Trials and Pharmacovigilance Unit of the DH (tel. no.: 2319 2920, fax: 2319 6319 or email: adr@dh.gov.hk). For details, please refer to the website at Drug Office under "ADR Reporting": http://www.drugoffice.gov.hk/adr.html. You may wish to visit the Drug Office's website for subscription and browsing of "Drug News" which is a monthly digest of drug safety news and information issued by Drug Office.

Yours faithfully,

(Terence MAN)
for Assistant Director (Drug)