

<04-Feb-2024>

Direct Healthcare Professional Communication (DHPC) Letter

ETOPOSID "EBEWE" 200MG)(20MG-ML) VIAL I.V. administration (not for Etoposide Phosphate containing products): Risk of infusion-related hypersensitivity reactions when administered with an in-line filter.

Dear Healthcare Professional,

This letter is sent in agreement between Sandoz and the SFDA to inform you the following:

Summary

An increased risk of infusion-related hypersensitivity reactions has been observed with the use of in-line filters during administration of etoposide-containing medicinal products.

- **It is currently unknown whether the risk increase occurs with all types of in-line filters or only with in-line filters made of certain materials.**
- **In-line filters should not be used.**
- **The above recommendations apply only to etoposide and not to etoposide phosphate. For medicines containing etoposide phosphate, filters should be used according to the information in the product information.**

Background on the safety concern

Etoposide-containing drugs are indicated for the treatment of various cancers in adults and children, including testicular cancer, small-cell lung cancer, Hodgkin's lymphoma, non-Hodgkin's lymphoma, acute myeloid leukemia, gestational trophoblastic neoplasia and ovarian cancer.

Some cytostatic require the use of in-line filters during application, according to the technical information and usage information. These filter systems are made up of various components and their main function is to retain particles¹. Various guidelines have recommended the use of in-line filters during continuous or intermittent infusion of etoposide-containing medicinal products². The SPC for medicines containing etoposide (except etoposide phosphate) does not mention the use of in-line filters. It is neither recommended nor prohibited. Therefore, it might be possible for in-line filters to be used according to local medical practice.

Studies have been published in the literature showing an increased risk of infusion-related hypersensitivity reactions when an in-line filter is used for administration^{3 4}. The exact mechanism behind this observation is not known, but it is suspected that the solubilizers used in etoposide-containing drugs interact with the filter or infusion system and that its components (e.g. plasticizers) dissolve.

Based on available literature data, European Medicine Agency (EMA)/ PRAC considers a causal relationship between the administration of drugs containing etoposide (not etoposide phosphate) with an in-line filter and the increased risk of hypersensitivity reactions to be at least possible.

Based on available information, the safety information in section 4.4 "Special warnings and precautions for use" of the SPC will be updated as appropriate to reflect the latest data and recommendations:

"An increased risk for infusion-related hypersensitivity reactions was observed when in-line filters were used during etoposide administration. In-line filters should not be used".

Reporting adverse events

Reporting suspected adverse reactions after approval is of great importance. It enables continuous monitoring of the benefit-risk ratio of the drug. Healthcare professionals are requested to report any suspected adverse reactions to the marketing authorization holder or to the Saudi Food & Drug Authority:-

Call for Reporting:

The National Pharmacovigilance Center

Unified Contact Center: 19999
Fax: +966112057662
Email: npc.drug@sfda.gov.sa
Website: <https://ade.sfda.gov.sa>

Sandoz Patient Safety Responsible

Reporting channels

Email: adverse.events.sau@sandoz.com
Website: <https://pvi1j.solutions.iqvia.com/pvi-web/>

Haya Fahad Bin Omar

Annexes

Updated section SmPC section 4.4

Risks and mitigation strategies to prevent etoposide infusion-related reactions in children.

Etoposide hypersensitivity reactions associated with in-line filter use: A retrospective cohort study at CHU de Québec-Université Laval

References

¹ **Kim** SH, Stollhof B, Krämer I. Selection and handling of in-line filters for parenteral administration of tumor therapeutics. Mainz, Germany: Hospital Pharmacy; 2018;39:11–18

² **BC** Cancer Agency. Provincial Pharmacy Directive III-50-04: Management of Particulate During Sterile Preparation. Vancouver, British Columbia: BC Cancer Agency; July 9, 2014.

³ **Tillman** EM, Suppes SL, Miles N, Duty AM, Kelley KL, Goldman JL. Risks and mitigation strategies to prevent etoposide infusion-related reactions in children. *Pharmacotherapy*. 2021 Aug;41(8):700-706. doi: 10.1002/phar.2603. Epub 2021 Jun 29. PMID: 34129705; PMCID: PMC8617599.

⁴ **Dodier** K, Laverdière I, Roy MJ. Etoposide hypersensitivity reactions associated with in-line filter use: A retrospective cohort study at CHU de Québec-Université Laval. *J Oncol Pharm Pract*. 2022 Dec 21:10781552221146801. doi: 10.1177/10781552221146801. Epub ahead of print. PMID: 36544381.