IMPORTANT WITHDRAWAL NOTICE
AmBisome Liposomal Amphotericin B 50mg Powder for Concentrate for Dispersion for Infusion (HA705) - Minisart® Filter

On 05 February 2021, Gilead Sciences Ltd. notified WHO that they had received a Field Safety Notice from their supplier, Sartorius, in relation to specific lots of 5µm sterile filter (medical device Minisart® Filter 17594-GJR) which is co-packed in cartons of AmBisome® product. Sartorius have informed Gilead that there is a potential that the filter lot packaged with the AmBisome® batches listed in the table below may be releasing intrinsic fibres and particles from the filter membrane, which may pose a risk to the patient.

The defect is specific to the filter. There is no quality defect with the AmBisome inside the packs. The overall probability of adverse health consequences due to the affected filters is low, however, if risk occurs, the severity of harm has the potential to be high. As stated by Gilead

> "*From a risk perspective, a preliminary Health Hazard Evaluation performed by Gilead has assessed the risk of thromboembolism associated with the use of AmBisome® with the affected filters in the indicated populations. The severity of harm (if risk occurs) is considered high, because the quality defect could potentially result in permanent impairment of body function or permanent damage to a body structure. AmBisome® is indicated in patients aged 1 month and older. The paediatric population is at greatest risk, and the quality defect is considered potentially life-threatening in this population. The likelihood of clinically relevant occurrence of the risk is considered low, given the small size of the identified particulates and the short-term anticipated period of exposure to AmBisome®. No evidence of increased adverse reaction reporting of either infusion-related reactions or thromboembolic events has been identified. While this does not confirm an absence of clinical sequelae, it supports the Gilead assessment that the overall probability of adverse health consequences is low.*"

List of AmBisome lots with impacted filters:

Lot Number	**Expiry Date**
D1900139D	30 Sep 2023
D2000004D	31 Dec 2023
019549D	31 Dec 2023
019549D1	31 Dec 2023
020595D	31 Dec 2023
020570D	31 May 2024

With reference to the AmBisome® lots listed, Gilead requests that:

> "*distribution is ceased with immediate effect and to put these batches in quarantine until replacement filters are available to be supplied with the product. Please do not open any impacted AmBisome® lots to change out the defective filters with the replacement filters. The original AmBisome® product must be given to customers, along with replacement filters*."

The recommended approach to manage this issue (and agreed by Gilead with the Regulatory Authority in the country of manufacture, Ireland (HPRA) to implement for the Irish market) is to notify all impacted stakeholders in the supply chain to hospital level of the issue, to ask the health care professionals (HCPs) to dispose of the impacted filters and to use alternative filters of equivalent specification, or replacement filters which can be sourced from Gilead and to require distributors/wholesalers to cease distribution of the impacted AmBisome lots (to be put in quarantine) until Gilead can provide replenishment filters. In addition, it is requested that AmBisome cartons not be opened at distributors/wholesalers to replace out the defective filters with new filters but rather for the distributors/wholesalers to send replacement filters, once available, with the impacted AmBisome batches.

Therefore, it is advised that this approach, as agreed with the Regulatory Authority in the country of manufacture, Ireland (HPRA), should be discussed within the regulatory authorities in all territories where affected lots have been distributed and the approach to be taken should be determined in each local market. Once agreed within the applicable regulatory authority, it is recommended to ensure that the product is quarantined and details of the AmBisome lots quarantined are provided to the authorities by distributors/wholesalers with HCP letters approved within each respective regulatory authority be provided to distributors/wholesalers for dissemination to end customers.

Further information:

Dr. Joey Gouws, Team Lead, Inspection Services
Prequalification Unit — Email: gouwsj@who.int; Tel: +41 79 2394143