Ifosfamide cancer medicines: EMA starts a review

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Information on ifosfamide

- Ifosfamide is a medicine used to treat various type of cancer including solid tumours and lymphomas (cancer of white blood cells)
- Ifosfamide is administered intravenously and it is available in different dosage forms within Europe including ready-made solution, concentrate for solution and a powder for solution for infusion.

In Malta Ifosfamide is authorised through a national procedure:

Active Ingredients	Product Name	Pharmaceutical Form	Classif-cation	Authorisation Number	MAH/license holder
Ifosfamide 2 gram(s)	Mitoxana 2 g Powder for Sterile Concentrate	Powder for concentrate for solution for infusion or injection	POM	MA1277/00701	Baxter Holding B.V.

Information from the EMA about risk of encephalopathy with ifosfamide

Following a request from France, the Pharmacovigilance Risk Assessment Committee (PRAC) has started a review on ifosfamide-containing medicinal products.

During the review it will be examined whether ifosfamide available as ready solution or concentrate for solution is related to higher risk of encephalopathy (brain disorder) than ifosfamide available as powder form. The risk of encephalopathy associated with ifosfamide is already known and reflected in the product information for these medicinal products.

A 3 to 4-fold higher risk of encephalopathy associated to the use of ready-made solution compared with the powder was observed in a review carried out in France in 2016. At the time the solution's shelf life was reduced in France due to probable association between the degradation of the active substance with subsequent development of impurities over time in the solution and the increased risk of

encephalopathy. However, in two recent studies[1, 2] it was observed that the risk of encephalopathy with the solution stays higher than the risk of encephalopathy with the powder.

The EMA will review available data on the risk of encephalopathy associated with the use of ifosfamide ready-made solution or concentrate for solution and recommend whether the marketing authorisations for these products should be maintained, varied, suspended or revoked.

PRAC's recommendation will be forwarded to the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) which will adopt a position.

For more information, visit the European Medicines Agency's Ifosfamide referral page

Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance on Ifosfamide-containing medicinal products. Suspected Adverse Drug Reactions (side effects) may be reported using the Medicines Authority Form and sending it to Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000 or online to **http://www.medicinesauthority.gov.mt/adrportal** or to the marketing authorisation holder or their local representatives.

Post-Licensing Directorate
Medicines Authority

Healthcare professionals and patients are encouraged to regularly check the Medicines Authority website for product safety updates as these are issued on an ongoing basis.

[1] Hillaire-Buys D, Mousset M, Allouchery M, et al. Liquid formulation of ifosfamide increased risk of encephalopathy: A case-control study in a pediatric population. Therapies [Online]. 2019 https://doi.org/10.1016/j.therap.2019.08.001

[2] Chambord J, Henny F, Salleron J, et al. Ifosfamide-induced encephalopathy: Brand-name (HOLOXAN®) vs generic formulation (IFOSFAMIDE EG®). J Clin Pharm Ther. 2019;44:372–380. https://doi.org/10.1111/jcpt.12823

Feedback Form

The Medicines Authority thanks you for the time taken to read this safety circular. The dissemination of safety circulars is an important process whereby Regulatory Authorities can communicate important issues with respect to the safety of medicines, in order to protect and enhance public health

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