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EMA starts review of certain ifosfamide cancer medicines

EMA has started a review of certain medicines containing ifosfamide to examine whether there is a higher risk of encephalopathy (brain disorder) with ifosfamide available as a ready-made solution or concentrate for solution than with the powder form.

Ifosfamide is used to treat different types of cancers, including various solid tumours and blood cancers such as lymphomas (cancer of white blood cells). The risk of encephalopathy is already known and reflected in the product information for these medicines.

In 2016, an investigation in France suggested an incidence of encephalopathy 3 to 4-fold higher with the ready-made solution than with the powder. Analyses carried out at the time concluded that the risk may be linked to the degradation of the active substance and impurities developing over time in the solution. As a result, the solution's shelf-life was reduced in France. However, two recent studies[1,2] suggested that the risk of encephalopathy with the solution remains higher than the risk with the powder and a more thorough review was considered needed.

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

More about the medicine

Ifosfamide is used to treat different cancers, including various solid tumours and lymphomas. It is given into a vein and is available as a ready-made solution, a concentrate for solution and a powder for solution for infusion in Germany and France. In most other EU Member States it is only available as powder for solution for infusion.

[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

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More about the procedure

The review of ifosfamide-containing medicines has been initiated at the request of France, under Article 31 of Directive 2001/83/EC.

The review is being carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines, which will make a set of recommendations. As ifosfamide-containing medicines are all authorised nationally, the PRAC recommendations will be forwarded to the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), which will adopt a position. The CMDh is a body representing EU Member States as well as Iceland, Liechtenstein and Norway. It is responsible for ensuring harmonised safety standards for medicines authorised via national procedures across the EU.