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IMPORTANT MEDICINE SAFETY INFORMATION

APPROVED BY THE HPRA

An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Valproate (Epilim▼):

NEW educational materials for MALE patients.

UPDATED educational materials for GIRLs and WOMEN OF CHILDBEARING POTENTIAL.

prevent
valproate pregnancy prevention programme

June 2024

Dear Healthcare professional,

Please find enclosed **new** valproate (Epilim) educational materials for **male patients** which have been developed to support the implementation of new precautionary measures for valproate use in male patients in clinical practice.

Please also find **updated** educational materials for **girls and women of childbearing potential** to support the implementation of the existing pregnancy prevention programme (known as 'prevent').

Valproate Use in Male Patients

New Educational materials for MALE patients:

Further to the Dear Healthcare Professional Communication (DHPC) dated 19th February 2024 regarding the introduction of new measures for valproate use in male patients, new educational materials are now available to support the implementation of these measures in clinical practice. These include:

- A **new male patient guide** which should be provided to all male patients treated with valproate. This guide provides information regarding the potential risk of neurodevelopmental disorders (NDDs) in children of fathers treated with valproate in the 3 months prior to conception.

- An **updated healthcare professional guide** that includes a dedicated section on male patients to inform healthcare professionals about the potential risk of NDDs following paternal exposure to valproate in the 3 months prior to conception and advice to provide to male patients and their female partners.

- An **updated patient card (attached to the outer packaging)** that includes information relating to the potential risk of NDDs in children of fathers treated with valproate in the 3 months prior to conception. As it will take several months for the outer packaging to include the updated patient card, copies of the updated patient card will be supplied to pharmacists in the interim to be given to male patients each time valproate is dispensed.

New measures for valproate use in MALE patients

- **It is recommended that in male patients valproate is initiated and supervised by a specialist experienced in treatment of epilepsy or bipolar disorder.**
- **Prescribers should inform male patients about the potential risk and discuss with them the need to consider effective contraception, including for a female partner, while using valproate and for 3 months after stopping the treatment;**
- **Treatment with valproate in male patients should be regularly reviewed by prescribers to evaluate whether valproate remains the most suitable treatment for the patient.**
- **For male patients planning to conceive a child, suitable alternative treatment options should be considered and discussed with the patient. Individual circumstances should be evaluated for each patient. It is recommended that advice from a specialist experienced in the management of epilepsy or bipolar disorder should be sought as appropriate.**
- **Male patients should be advised to not donate sperm during treatment and for at least 3 months after treatment discontinuation.**
- **The male patient guide should be provided to male patients.**
- **The updated patient card will be attached to the outer packaging and male patients should be alerted to it with each dispensing. In the interim, the updated patient card should be provided to male patients each time valproate is dispensed.**
- **Male patients should receive a copy of the package leaflet with each dispensing.**

Valproate Use in Girls and Women of Childbearing Potential

Updated educational materials for GIRLs and WOMEN OF CHILDBEARING POTENTIAL:

Following the evaluation of an EU survey of healthcare professionals and patients to assess the effectiveness of the existing risk minimisation measures for girls and women of childbearing potential, the EMA recommended updates to the healthcare professional guide and the female patient guide. These updates were recommended to further enhance the knowledge on the known of risks of valproate exposure in-utero (teratogenic and NDDs), adherence to prescribing conditions and the pregnancy prevention programme. There have been **no changes to the safety information** presented in the guides.

- The **healthcare professional guide** has been restructured to support knowledge improvement, with sections divided according to the role of the healthcare professional and indication, to improve understanding, visualisation and navigation.

- The **female patient guide** has been revised so that it is easier to read, with the inclusion of flow charts and illustrations.

The **annual risk acknowledgement form** remains unchanged.

For girls and women of childbearing potential, healthcare professionals are reminded that:

- **Valproate must be initiated and supervised by a specialist experienced in the management of epilepsy or bipolar disorder. A specialist is defined as a consultant psychiatrist or a consultant neurologist who regularly manages bipolar disorder or complex epilepsy.**
- **Valproate should not be used in female children, girls and women of childbearing potential unless other treatments are ineffective or not tolerated.**
- **Valproate is highly teratogenic. Children exposed to valproate in utero are at high risk of NDD (in up to 30-40% of cases) and of major congenital malformations (in approximately 11% of cases).**
- **In bipolar disorder, valproate is contraindicated in pregnancy.**
- **In epilepsy, valproate is contraindicated in pregnancy unless there is no suitable alternative treatment.**
- **In any indication, valproate is contraindicated in women of childbearing potential, unless all the conditions of the pregnancy prevention programme 'prevent' are met.**

- **Conditions include assessment of potential for pregnancy, pregnancy testing, use of effective contraception, review of treatment at least annually and when planning a pregnancy or if pregnancy occurs. Female patients of childbearing potential should be counselled to ensure that they understand and acknowledge the risks of congenital malformations and neurodevelopmental disorders including the magnitude of these risks for children exposed to valproate in utero.**
- **These measures are described in the product information for Epilim and in the enclosed educational materials.**

Please refer to the Epilim healthcare professional guide and the Summary of Product Characteristics for further information on the role of specialists, GPs and pharmacists when treating males, girls and women of childbearing potential on valproate.

Education Materials Contents Enclosed for use in your Clinical practice:

- 1 **updated** healthcare professional guide – now includes a dedicated section on the use of valproate in male patients, as well as guidance on the actions for healthcare professionals on implementing the pregnancy prevention programme for girls and women of childbearing potential.
- 10 **new male** patient guides – to be provided to all male patients prescribed valproate (Epilim) and should be used when discussing the risks of exposure to valproate in male patients in the 3 months before conception.
- 5 **updated** female patient guides – to be provided to all girls and women of childbearing potential prescribed valproate (Epilim) and should be used when discussing the risks of exposure to valproate during pregnancy. An interactive version of this guide is available on the HPRA website, as outlined below.
- 5 annual risk acknowledgment forms - to be discussed and completed by the specialist with all female patients of childbearing potential treated with valproate (Epilim) – at treatment initiation (or when menarche is reached), at each annual visit, when a pregnancy is planned or if a pregnancy occurs. An interactive version of this form, which can be completed online and printed for final signature, is available on the HPRA website, as outlined below.
- 5 **updated** patient cards - pharmacists should ensure a patient card is provided to both **male** and **female patients** each time valproate (Epilim) is dispensed. The outer carton for Epilim products will be revised to include this updated patient card.

Electronic versions of these materials are also available on www.hpra.ie (enter 'Epilim' or 'valproate' in the 'Find a medicine' search box and click on 'EdM' next to any of the medicines that appear). Additional hardcopy versions of the materials can be ordered at any time by contacting Sanofi Medical Information on Tel: (01) 403 5600 or e-mail: IEMedinfo@sanofi.com

Call for reporting

Valproate (Epilim▼) is subject to additional monitoring.

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance. Website: www.hpra.ie

Adverse events should also be reported to Sanofi Ireland Ltd. Tel: 01 403 5600. Alternatively, send via email to IEPharmacovigilance@sanofi.com.

Yours faithfully

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