Important Safety Information – Action needed – Please Read

Valproate medicines: only for use when no other treatment is effective or tolerated in girls, women of childbearing age, and women who are pregnant or planning pregnancy; important actions required

This letter is for specialists and specialist nurses/midwives managing patients treated with valproate-based medicines (sodium valproate [Epilim▼, Episenta▼]; valproic acid, sodium valproate [Epilim▼]; valproate semisodium [Depakote▼]), and general practitioners who provide primary care to these patients.

Dear Healthcare Professional

This letter is sent in follow-up to the communication issued by the Medicines and Healthcare products Regulatory Agency in January 2015, and a further mailing on behalf of all valproate manufacturers in February 2016. It supplements the Patient Safety Alert on valproate issued by the MHRA and NHS Improvement on 6 April 2017 and those subsequently sent in Scotland, Wales and Northern Ireland. Previous communications advised that **valproate should only be used in girls, women of child bearing age and those who are pregnant or planning pregnancy when no other treatment is effective or tolerated.** This is because **children exposed in utero to valproate are at a high risk of serious developmental disorders (in up to 30–40% of cases) and/or congenital malformations (in approximately 10% of cases).**

Despite these communications, valproate continues to be used frequently in this patient group. A recent survey of women of childbearing age taking valproate for epilepsy has identified that 20% had not been informed of these risks and 80% had not received any written information from their HCPs. Prescribing data show little change in the rate of prescription of valproate to girls and women of childbearing age since 2015, regardless of the indication. **A significant number of patients remain at risk of inadvertent exposure to valproate in pregnancy and further efforts and actions are needed from prescribers and dispensers of valproate to reduce the risks that this entails**.

Please turn over to see the actions that you are being asked to perform.

THE RISK: Children exposed in utero to valproate are at a high risk of serious developmental disorders (in up to 30–40% of cases) and/or congenital malformations (in approximately 10% of cases).

For this reason, you are asked to take the following actions:

- **DO NOT prescribe valproate to female children, female adolescents, women of childbearing potential, or pregnant women UNLESS other treatments are not effective or other treatments are not tolerated.**

- **ONLY doctors experienced in managing epilepsy or bipolar disorder should prescribe valproate to these patients, and must supervise ongoing treatment with a review annually, at a minimum.**

- **If you prescribe valproate YOU MUST INFORM all girls and women of childbearing age of the following, and ensure the information is understood:**
    1. **the risks to a baby from taking valproate during pregnancy;**
    2. **the need to use effective contraception while taking valproate;**
    3. **the need for regular (at least annual) review of treatment;**
    4. **the need to rapidly consult you if planning a pregnancy or becomes pregnant**

- **If you are a General Practitioner caring for girls or women of childbearing age taking valproate, YOU MUST ENSURE that your patient is seen by the specialist responsible for prescribing valproate at least annually, and as a matter of urgency if she is planning pregnancy or becomes pregnant.**

To support effective prescribing practice, the enclosed booklet "Important Information for Healthcare Professionals on the Risks of Valproate in Female Patients" provides information on the risks and actions you are required to take.

Also enclosed is an information booklet to provide to patients: "Valproate Patient Guide". This is intended to be distributed by specialists initiating and supervising treatment with valproate, and you should give a copy to every girl or woman of childbearing age taking valproate. In addition, General Practitioners and Pharmacists are encouraged to provide copies to these patients who are not already aware of the information, alongside a reminder card provided by pharmacists when valproate is dispended.

Additional copies of both booklets can be ordered, at no cost, by contacting Sanofi Medical Information on 0845 372 7101 or by emailing UK-medicalinformation@sanofi.com. They can also be downloaded from the EMC website (www.medicines.org.uk) where they will be found linked with entries for medicines containing valproate.

Finally, a checklist has been developed to use during patient consultations. This will help ensure that the key points regarding the risks of valproate are discussed with the patient, and then when valproate is prescribed it is not being used inappropriately. This should be used with every girl and women of childbearing age when valproate is FIRST PRESCRIBED and at EVERY subsequent review, at least annually.

The checklist is printed at the end of this letter, and additional copies can be downloaded from the EMC website (www.medicines.org.uk) where they will be found linked with entries for medicines containing valproate.

You may find it helpful to keep this letter, and refer especially to pages 2 and 4 when initiating or reviewing valproate in girls and women of childbearing age. It may be helpful to display these two pages as a ready reference for relevant prescribers.

Call for reporting:
All valproate-containing drugs are subject to additional monitoring. Any suspected adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to the pharmaceutical company proving the valproate preparation, contactable at the address indicated on the packaging, in the Summary of Product Characteristics or Patient Leaflet, or in the BNF.

Thank you for your co-operation in following these requirements. This will help ensure appropriate use of valproate in this patient group and minimise these significant risks.

Yours faithfully

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This letter is sent at the request and with the approval of the Medicines and Healthcare products Regulatory Agency.

Treatment with valproate for female patients: Checklist for patients and prescribers

A. Checklist for Prescribers

Name of Patient /carer
I confirm that the above named patient does not respond adequately or tolerate other treatments or medical treatments and requires valproate ☐

I have discussed with the above named Patient/carer:

The overall risks of an approximately 10% chance of birth defects and up to 30–40% chance of a wide range of early developmental problems that can lead to significant learning difficulties in children exposed to treatment with valproate during pregnancy. ☐
Individual risk can be minimised by use of the lowest possible effective dose ☐
The need for contraception (if child bearing age) ☐
The need for regular review of the need for treatment ☐
The need for urgent review if the patient is planning a pregnancy ☐
I have given the patient/carer a copy of the patient information booklet ☐

Name of Prescriber **Date**

B. Patient /Carer Checklist

I understand:
Why treatment with valproate rather than another medicine is considered necessary for me ☐
The risks of an approximately 10% chance of birth defects and up to 30–40% chance of a wide range of early developmental problems that can lead to significant learning difficulties in children exposed to treatment with valproate during pregnancy. ☐
That I am advised to use contraception if not planning a pregnancy ☐
That my treatment should be reviewed regularly ☐
That I should request an urgent review if planning a pregnancy PRIOR to attempting to conceive ☐

Name of Patient/ Carer **Date**
