Medicines & Healthcare products Regulatory Agency

MHRA
Regulating Medicines and Medical Devices

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151 Buckingham Palace Road
London
SW1W 9SZ
United Kingdom
www.gov.uk/mhra

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Valproate and risk of abnormal pregnancy outcomes: new communication materials

Dear Healthcare Professional,

In January 2015 we wrote to inform you that children exposed to valproate in utero are at high risk of developmental disorders and congenital malformations. To further improve awareness of the risks of valproate in pregnancy we are asking that you use the new communication materials below to support discussion of these risks with women of childbearing potential and girls who take valproate. Hard copies are being sent to relevant healthcare professionals from this week.

Resources to use (see below for more information):

- Booklet for healthcare professionals
- Consultation checklist
- Guide to give to patients
- Card to give to patients

Later in 2016, the outer packaging for medicines containing valproate will include a warning for women on the risk of adverse pregnancy outcomes.

Summary of risks and precautions

- Children exposed in utero to valproate are at a high risk of serious developmental disorders (in up to 30-40% of cases) and congenital malformations (in approximately 10% of cases) refs1-9
- Valproate should not be prescribed to female children, female adolescents, women of childbearing potential or pregnant women unless other treatments are ineffective or not tolerated.
- Valproate treatment must be started and supervised by a doctor experienced in managing epilepsy or bipolar disorder.
- Carefully balance the benefits of valproate treatment against the risks when prescribing valproate for the first time, at routine treatment reviews, when a female child reaches puberty and when a woman plans a pregnancy or becomes pregnant.
- You must ensure that all female patients are informed of and understand:
  - risks associated with valproate during pregnancy;
  - need to use effective contraception;
  - need for regular review of treatment;
  - the need to rapidly consult if she is planning a pregnancy or becomes pregnant

For specialists (neurologists, psychiatrists and paediatricians)

We are asking that you use the following resources to help manage and minimise the risks outlined above. If you manage specialist care in your organisation, ensure that processes are in place to allow these requirements to be met.

Healthcare professional booklet
Read the healthcare professional booklet which gives:

- a comprehensive overview of the risks of valproate in females of childbearing potential and during pregnancy,
- points to consider and steps to take when deciding to treat women of childbearing potential and girls with valproate.

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Checklist
Whenever you conclude it necessary to treat or continue treating a woman of childbearing potential or girl with valproate, use the checklist to check that you have given her all the necessary information and that she has fully understood it. Add the completed checklist to her medical records as a permanent record of your discussion.

Patient guide
When considering treating a woman of childbearing potential or girl with valproate, give her or her carer the valproate patient guide and ensure that she understands the information it contains.

Paediatricians should also refer parents or carers to the Royal College of Paediatrics and Child Health information about valproate (via http://www.medicinesforchildren.org.uk/sodium-valproate-preventing-seizures).

For general practitioners
Valproate treatment must be started and supervised by a specialist experienced in managing epilepsy or bipolar disorder. Consider the need to arrange treatment reviews with the relevant specialist for women of childbearing potential and girls who are currently taking valproate. If a woman who is taking valproate tells you she is pregnant or would like to have a baby, refer her to the specialist responsible for her care.

For pharmacists

Patient card
Whenever you dispense valproate for a woman of childbearing potential or girl, give her a patient card which summarises the important information she needs to know about taking valproate. If you manage dispensing services in your organisation, ensure that processes are in place to allow these requirements to be met.

Off-label use: risks and advice still apply
Valproate is not licensed for treatment of conditions other than epilepsy or bipolar disorder in the UK. However, we are aware that these medicines are sometimes used 'off-label' (eg for migraine or chronic pain). If you are considering initiating or continuing such treatment, the same risks and advice in this letter apply.

Monitoring effectiveness
The effectiveness of the above risk minimisation measures will be continuously monitored via prescribing data and evaluation of levels of patient awareness. Results will be communicated as they become available. As with all medicines, we will continue to monitor the safety and efficacy of valproate to assess the need for further regulatory action.

As with all medicines we request that you report suspected adverse drug reactions, including those suspected in a baby or child to result from in utero exposure to a medicine taken by a mother, via the Yellow Card scheme https://yellowcard.mhra.gov.uk.

Yours sincerely,

June M. Raine

Dr June Raine
Director, Vigilance and Risk Management of Medicines Division
Telephone: +44(0)203 080 6000
Email: info@mhra.gsi.gov.uk

Links to electronic copies of resources
Healthcare professional booklet
www.medicines.org.uk/emc/RMM.420.pdf
Patient guide www.medicines.org.uk/emc/RMM.421.pdf
Checklist www.medicines.org.uk/emc/RMM.423.pdf
Patient card www.medicines.org.uk/emc/RMM.422.pdf

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