

## BMJ Letter

### Valproate, women and exceptional circumstances

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***The Medicines and Healthcare products Regulatory Agency (MHRA) regulations now require an annual signed confirmation of adherence to the Pregnancy Prevention Programme in women of child-bearing potential taking valproate. MHRA acknowledge that for some women with epilepsy, it valproate discontinuation may not be possible and they may have to continue treatment (with appropriate specialist care) in pregnancy (1). We outlined in an open letter to the MHRA exceptional circumstances when, despite childbearing potential, a pregnancy prevention programme is inappropriate, although a risk acknowledgment form is still required (BOX online). These include emergency situations (e.g. status epilepticus); fully-informed women deciding on valproate who may or may not become pregnant (2, 3, 4); those lacking capacity (e.g. intellectual disability), where a best interest process supports Valproate continuation. This guidance is endorsed by the Royal College of Psychiatrists Intellectual Disability Section, the United Kingdom Learning Disability Professional Senate and 61 individual epilepsy clinicians.***

#### References

1. Medicines and Healthcare products Regulatory Agency. <https://www.gov.uk/drug-safety-update/valproate-medicines-epilim-depakote-contraindicated-in-women-and-girls-of-childbearing-potential-unless-conditions-of-pregnancy-prevention-programme-are-met>.
2. Sisodiya SM and Epilepsy Advisory Group for the Association of British Neurologists. Valproate and Childbearing regulations. *Practical Neurology* 2018; 18:176-8
3. Angus-Leppan H, Liu RSN. Weighing the risks of valproate in women who could become pregnant. *BMJ* 361, k1596
4. Wright J. New restrictions on epilepsy drug may do more harm than good. 2018 - [spectrumnews.org. new-restrictions-on-epilepsy-drug-may-do-more-harm-than-good%20\(3\).pdf](https://www.spectrumnews.org/new-restrictions-on-epilepsy-drug-may-do-more-harm-than-good%20(3).pdf)

BOX (ONLINE SUPPLEMENTARY)

**Valproate post MHRA use: suggested guidance on exceptional circumstances**

The MHRA have issued new regulations regarding the use of valproate (<https://www.gov.uk/drugsafety-update/valproate-medicines-epilim-depakote-pregnancy-prevention-programme-materials>).

Its use will be banned in women and girls of child bearing potential unless they adhere to the Pregnancy Prevention Programme, to prevent the development of foetal abnormalities. There is international consensus that valproate is a significant teratogen, that alternatives should be offered where possible and safe, and that all women in whom it is considered need specialist review.

The MHRA recognises that in some women with epilepsy valproate cannot be stopped during pregnancy without major risk to the person and the unborn child (both frequent convulsions and convulsive status epilepticus are potentially dangerous to both mother and child). This paper outlines the situations in which a child or woman or her authorised representative may decide that she will continue valproate even though she might be, or may become, pregnant, and when the pregnancy prevention programme is not appropriate, although a risk acknowledgement form would still be required.

### 1. Emergency situations

- Status epileptics or serial seizures in a female of childbearing potential when valproate is considered by her medical specialists to be the most effective medication to control her seizures.
- In this situation discussion with the patient is usually not possible so treatment is given on a best interest basis under mental capacity legislation. Informed discussions about continuation of valproate and the associated risks would be undertaken on recovery with her, and / or her advocates, where capacity is impaired. Consent would be sought at a later date from the patient.

2. Epilepsy in a female of childbearing potential in whom valproate is the most effective medication and the fully informed woman decides it is the best option for her, and for whom the Pregnancy Prevention programme is not appropriate.

- This may follow unsuccessful trials of other medication.
- It may be in women who are currently seizure free on valproate as first line monotherapy, and who, after fully informed discussion, do not wish to change to another medication because of the risks to their personal safety of switching to an alternative.
- Women who are not able to become pregnant for health-related or physical reasons
- Women who, after fully informed discussion, do not wish to use the forms of contraception recommended by the MHRA for personal, religious or health reasons.

3. In those who may lack capacity, such as some women with intellectual disability, an individual assessment of abilities to make informed choices on epilepsy management and medication issues is needed.

- In some women with moderate to profound intellectual disability consent to sexual intercourse may be unlikely, so pregnancy is not likely to occur (in these women pregnancy would raise significant concerns of abuse, sexual exploitation or rape).
- Pregnancy prevention may be part of the care plan to manage psychological distress arising from menstruation in women with moderate to profound intellectual disability lacking mental capacity to understand the natural physiological changes.

- Those with mild Intellectual Disability should be managed as other women are, but will need particular care to support their decisions in this area and may require augmented communication to enable them to make informed decisions on using medication. There may need to be involvement of special parenting services in addition to other key stakeholders such as social care.

### **Individual signatories**

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