



# Sodium Valproate Update October 2018

prevent valproate  
pregnancy prevention  
programme

Reference: Drug Safety Update  
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# Background



- The pregnancy prevention programme (PPP) applies to:
  - Sodium valproate: indicated for various forms of epilepsy.
  - Semisodium valproate (valproic acid): indicated for mania in bipolar disorder where lithium cannot be used.
  - Unlicensed uses of the above.
- This programme provides an update to the MHRA alert '*Resources to support the safety of girls and women who are being treated with valproate*' (NHS/PSA/RE/2017/002), issued in 2017.

# prevent valproate pregnancy prevention programme (PPP)



- In March 2018 the CMDh\* endorsed a strengthened regulatory position on valproate medicines. Valproate must no longer be used in any woman or girl able to have children unless there is no other alternative and she has a pregnancy prevention programme in place. This is designed to make sure patients are fully aware of the risks and the need to avoid becoming pregnant.

\* The CMDh is a medicines regulatory body representing the European Union (EU) Member States, Iceland, Liechtenstein and Norway.

# Background



- These new regulatory measures also include a ban on the use of valproate for migraine or bipolar disorder during pregnancy, and a ban on the use of valproate to treat epilepsy during pregnancy unless there is no other effective treatment available
- Updated actions have also been agreed with specialist trusts
- Focusing particularly on the guidance for general practitioners, we have suggested actions and identified resources locally and from the toolkit to support you.

# Continued Primary Care Actions - Highly effective contraception



- Highly effective contraception is considered for regulatory purposes to be those user independent methods such as the long acting reversible contraceptives (LARC), copper intrauterine device (Cu-IUD), levonorgestrel intrauterine system (LNG-IUS) and progestogen only implant (IMP) and female sterilisation, all of which have a failure rate of less than 1% with typical use.
- Failure rate will increase if contraception given out with recommended timeframes.
- Vasectomy – less than 1% failure rate – patient still needs informed in case circumstances change.
- Subcutaneous Sayana Press self administration – awaiting confirmation from MHRA.
- Be mindful of patients with learning disabilities – they may still need contraception.

# Updated Primary Care Actions



- Inform patient of the known risks and ensure that she understands she must not get pregnant whilst taking valproate – provide patient guide.
- Tell her to contact you immediately if she suspects there has been a problem with her contraception or she may be pregnant
- Check she is using contraception and understands the need to comply with contraception throughout treatment and undergo pregnancy testing when required – e.g. if there is any reason to suggest lack of compliance or effectiveness of contraception.
- **Inform her that she will need to see a specialist at least every year while taking valproate medicines and arrange for referral.**
- **Refer her to specialist (unless she has seen one recently and is already on prevent)**

# Referral to specialist



## ARAF – Annual Risk Acknowledgment Form

Referral Criteria	Recommended Referral
Age 8-18	Local paediatrician (NCUHT). Referral to the epilepsy clinic is via the e-referral system – Add to e-referral ' <b>Referral is for valproate review and completion of ARAF, shared back to GP</b> '. Local paediatrician UHMBT or Newcastle Hospitals - use usual referral mechanism making clear ' <b>Referral is for valproate review and completion of ARAF, shared back to GP</b> '
Age 19+ Learning Disability	Community Learning Disability Team (CPFT). Referral to Learning Disabilities is via standard referral form. Add to standard referral form ' <b>Referral is for valproate review and completion of ARAF, shared back to GP</b> '
Age 19+ Bipolar diagnosis or other mental health diagnosis	CMHART (CPFT). Referral is via standard <b>prevent valproate pregnancy prevention review form</b> which is solely for referral for valproate review.
Age 19+ Epilepsy Diagnosis	Neurology (CPFT). Please email the standard referral form to neurology. Add to the standard referral form ' <b>Referral is for valproate review and completion of ARAF, shared back to GP</b> '
Age 19+ Other Diagnosis. E.g. Migraine	Neurology (CPFT). Please email the standard referral form to neurology. Add to the standard referral form ' <b>Referral is for valproate review and completion of ARAF, shared back to GP</b> '

# Referral timescale



- In order to prioritise patient reviews and work with services in a joined up manner please refer those in age group 8-44 first. A date of the 1<sup>st</sup> December 2018 onwards has been agreed for these first referrals. From February 1<sup>st</sup> 2019 refer ladies with no menopause, age 45+.

Referral criteria	When to refer
Age 8-44	From 1st December 2018
Age 45+	From 1st February 2019

# After Specialist review- Primary Care Actions



After specialist review ensure:

- She is on prevent - the valproate pregnancy prevention programme and has a copy of the patient guide.
- She has a copy of the Annual Risk Acknowledgment Form signed by the specialist
- You file a copy of the signed Annual Risk Acknowledgment Form in her medical records.
- You update directions of medication to include 'PPP review month year' E.g. 'One to be taken twice a day. PPP review December 2019.'
- *This will ensure all health professionals across the interface have information available to them about the patient's status within their PPP. (Community/hospital pharmacists for dispensing and other specialists/services that may review the patient).*

# Following PPP commencement - Primary Care Actions



- Check that all patients have an up to date, signed, Annual Acknowledgment of Risk Form each time a repeat prescription is issued
- If there should be a lapse in a patients PPP review being updated annually in a timely manner (it is expected patients will be recalled through usual hospital procedures), ensure the patient is referred back to the specialist for review.
- Refer back to the specialist urgently (within days) in case of unplanned pregnancy or where a patient wants to plan a pregnancy.

# Following PPP commencement - Primary Care Actions



- A woman of childbearing potential is defined as a pre-menopausal female who is capable of becoming pregnant. These women need to be on the prevent - valproate pregnancy prevention programme, regardless of personal circumstances with respect to the potential of becoming pregnant , which may be subject to change.

# Primary Care Actions – Medication Review



Age range	Suggested approach for Medication review
<b>8-13</b>	Set an expectation with patients, parent and carers that this is not a medicine that would be continued when/if you decide to have a baby. Provide information to patient as appropriate to age/understanding. Should girls in this age band start periods manage as for 14-44.
<b>14-44</b> <b>Childbearing potential</b>	Provide information to patient as per suggested resources. Write to patients and use combination of face to face, telephone reviews as appropriate. Check she is using highly effective contraception. Ensure there is an up to date Annual Acknowledgment of Risk Form in the patient's records.
<b>45-60 No Menopause or no hysterectomy.</b>	Potential for pregnancy so manage as per Age 14-44.
<b>45-60 Menopause</b>	No action needed.

- At the medication review, ensure that women of childbearing age understand the risks of taking valproate in pregnancy and are using highly effective contraception. Refer to family planning services if required.

# Summary of Primary Care Actions



- Use the **Valproate patient guide**
- File the **Annual Risk Acknowledgement Form** in patient records
- Use the following system codes to record the consultation on clinical system:
  - Patients with epilepsy:
    - 6110 - contraceptive advice for patients with epilepsy
    - 8BIF - epilepsy medication review
  - Patients with mental health conditions:
    - 611 – general contraceptive advice
    - 8BMO – mental health medication review.
- If a woman who is taking valproate tells you she is pregnant or would like to have a baby, urgently refer her to the specialist responsible for her care so that a plan can be made for management during her pregnancy.

# Community Pharmacy Actions



- Ensure the Patient Card is provided every time valproate is dispensed
- Remind patients of the risks in pregnancy and the need for highly effective contraception.
- Ensure the patient has received the Patient Guide.
- Remind patients of the need for annual specialist review
- Dispense valproate in the original package. In situations where repackaging cannot be avoided always provide a copy of the package leaflet and add a sticker with the warning to the outer box
- If a woman of childbearing potential reports that she is not taking highly effective contraception, refer them to their GP (including by contacting the GP if necessary).

# Summary



- Help ensure that all women of child bearing potential understand risks of valproate and are taking adequate contraception by following new Valproate toolkit .
- For any young girls prescribed Valproate set an expectation that this is not a medicine that you would keep taking if/when you decide to have a baby. Ensure enrolled on prevent PPP at the appropriate time.
- Refer women wanting to have a baby or who finds out they are pregnant to specialist urgently.

# References



- Advice for women and girls taking valproate medicines - 24 April 2018. Medicines & Healthcare Regulatory Agency.  
<https://assets.publishing.service.gov.uk/media/5ade0039e5274a0d820946a6/Valproate-patient-DSU-for-pub-without-watermark.pdf>
- Guidance - Valproate use by women and girls – 18<sup>th</sup> May 2018. Medicines & Healthcare Regulatory Agency  
<https://www.gov.uk/guidance/valproate-use-by-women-and-girls>
- Chief Medical Officer Alert: Valproate contraindicated in women of childbearing potential unless there is a Pregnancy Prevention Programme CEM/CMO/2018/001 Date of issue: 24 April 2018
- [https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAttachment.aspx?Attachment\\_id=103004](https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAttachment.aspx?Attachment_id=103004)

# References



- Valproate medicines (Epilim ▼ , Depakote ▼): contraindicated in women and girls of childbearing potential unless conditions of Pregnancy Prevention Programme are met. Drug Safety Update - 24 April 2018. Medicines & Healthcare Regulatory Agency.
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