

# Valproate Existing and New recommendations for Primary Care

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The [MHRA's guidance](#), which applies across the UK, is that valproate must not be used in women of childbearing potential unless a Pregnancy Prevention Plan is in place. This is due to the risk of birth defects and developmental disorders in babies born to women who take valproate during pregnancy. There are specific actions for specialists, GPs and dispensers.

•According to guidance from the MHRA and pan-collegiate guidance endorsed by the Royal College of GPs, GPs have responsibility for:

- identifying and recalling all patients taking valproate who may be of childbearing potential
- providing them with the valproate patient guide
- checking they have been reviewed by a specialist in the last year (i.e. they have an in-date Annual Risk Acknowledgement Form)
- checking they have a Pregnancy Prevention Plan and are on highly effective contraception.
- GPs must identify and recall all women and girls who may be of childbearing potential, provide the Patient Guide and check they have been reviewed by a specialist in the last year and are on highly effective contraception (see later for information on contraception)
- <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>

- **Conditions and guidance for the Pregnancy Prevention Programme**
- All women and girls of childbearing potential being treated with valproate medicines must be supported on a Pregnancy Prevention Programme. These conditions are also applicable to female patients who are not sexually active unless the prescriber considers that there are compelling reasons to indicate that there is no risk of pregnancy.
- The Pregnancy Prevention Programme is a system of ensuring all female patients taking valproate medicines:
  - have been told and understand the risks of use in pregnancy and have signed a Risk Acknowledgement Form
  - are on highly effective contraception if necessary
  - see their specialist at least every year

- identify all patients taking valproate confirm indication and specialist who is sharing care.
- Confirm all valproate patients have an annual practice review including; Liver function which should be measured before therapy and then periodically monitored during the first 6 months of therapy, especially in those who seem most at risk, and those with a prior history of liver disease.
- Amongst usual investigations, tests which reflect protein synthesis, particularly prothrombin rate, are most relevant.
- Confirmation of an abnormally low prothrombin rate, particularly in association with other biological abnormalities (significant decrease in fibrinogen and coagulation factors; increased bilirubin level and raised transaminases) requires cessation of valproate therapy.

- Ensure all prescriptions for valproate are prescribed as a quantity which is a multiple of 30 and dispensed as a special container
- For any new patient <55 (male or female) where shared care of valproate is requested confirm request includes confirmation that two specialists have independently considered and documented that there is no other effective or tolerated treatment, or there are compelling reasons that the reproductive risks do not apply.
- Confirm all women of childbearing potential and girls prescribed valproate have been reviewed by a specialist in the last year (i.e. they have an in-date Annual Risk Acknowledgement Form)
- Confirm they have a Pregnancy Prevention Plan and are on highly effective contraception unless there are compelling reasons that the reproductive risks do not apply
- Ensure patients records are coded appropriately

[Valproate \(Belvo, Convulex, Depakote, Dyzantil, Epilim, Epilim Chrono or Chronosphere, Episenta, Epival, and Syonell ▼\): new safety and educational materials to support regulatory measures in men and women under 55 years of age - GOV.UK \(www.gov.uk\)](#)

<https://www.gov.uk/government/news/mhra-instructs-health-organisations-to-prepare-now-for-new-measures-to-reduce-ongoing-serious-harms-of-valproate>

### **Advice for healthcare professionals:**

- valproate must not be started in new patients (male or female) younger than 55 years, unless two specialists independently consider and document that there is no other effective or tolerated treatment, or there are compelling reasons that the reproductive risks do not apply. For the majority of patients, other effective treatment options are available
- at their next annual specialist review, women of childbearing potential and girls receiving valproate should be reviewed using the revised valproate Annual Risk Acknowledgement Form. A second specialist signature will be needed if the patient is to continue on valproate, however subsequent annual reviews will only require one specialist
- general practice and pharmacy teams should continue to prescribe and dispense valproate and if required offer patients a referral to a specialist to discuss their treatment options. Valproate should be dispensed in the manufacturer's original full pack

To support the implementation of these measures for valproate, the following safety and educational materials are available:

- [Patient guide](#): Provides those taking valproate (or their parent, caregiver, or responsible person) with information on the risks of valproate in pregnancy and the risks to male patients and what they need to do.
- [Healthcare Professional Guide](#): Provides updated information for healthcare professionals on the risks of valproate in pregnancy and the risks for male patients, the new conditions for valproate prescribing and key points for patient discussions.
- [Annual Risk Acknowledgement Form](#): For female patients starting valproate and at annual review. Used to support and record the discussion between the patient and specialist prescriber on the risks associated with valproate in pregnancy and to record the decision of the countersigning specialist. At subsequent annual reviews only one specialist is required.
- [Risk Acknowledgement Form for male patients starting valproate](#): Used to support and record the discussion between the patient and specialist prescriber of the risks associated with valproate in males when starting treatment with valproate and to record the decision of the countersigning specialist. This is only to be completed at initiation of valproate.
- [Patient card](#): Provides key information for female patients receiving valproate on contraception and pregnancy prevention.
- [Pharmacy poster](#): Provides important actions for pharmacists dispensing valproate to female patients.
- [Warning stickers](#): To be added to packaging of medicine in exceptional circumstances where the original pack cannot be dispensed.

See [Product Information](#) for valproate medicines, including the Patient Information Leaflet.

### Migraine Prophylaxis patients

- Latest Neurology advice;
- In patients <55 (male or female) taking valproate for migraine prophylaxis consider gradual withdrawal over 1 month of valproate in discussion with the patient
- Should migraines increase following cessation of valproate seek specialist advice and guidance and if required refer patient into headache pathway
- If migraine prophylaxis deemed clinically necessary specialist may recommend alternative suitable therapeutic options as per NICE guidance and formulary.



### Epilepsy patients

- Epilepsy Patients on valproate must be informed to not stop taking their treatment without advice from their specialist
- Confirm Epilepsy patients taking valproate are scheduled for an annual specialist review
- specialists must book in review appointments at least annually with women and girls under the Pregnancy Prevention Programme and re-evaluate treatment as necessary; explain clearly the conditions as outlined in the supporting materials; and complete and sign the Risk Acknowledgement Form—copies of the form must be given to the patient or patient/caregiver/responsible person and sent to their GP
- Prioritise referral of epilepsy patients prescribed valproate who are women of childbearing potential and girls and have no record of an annual specialist review in the last 12 month and/or no record of a risk acknowledgement form
- At their next annual specialist review (2024 onwards), women of childbearing potential and girls should be reviewed using a revised valproate Risk Acknowledgement Form, which will include the need for a second specialist signature if the patient is to continue with valproate and subsequent annual reviews (2025 onwards) with one specialist unless the patient's situation changes

### Bipolar and other MH patients

- Bipolar and other MH patients on valproate must be informed to not stop taking their treatment without advice from their specialist
- Confirm Bipolar and other MH patients taking valproate are scheduled for an annual specialist review
- specialists must book in review appointments at least annually with women and girls under the Pregnancy Prevention Programme and re-evaluate treatment as necessary; explain clearly the conditions as outlined in the supporting materials; and complete and sign the Risk Acknowledgement Form—copies of the form must be given to the patient or patient/caregiver/responsible person and sent to their GP
- Prioritise referral of Bipolar and other MH patients prescribed valproate who are women of childbearing potential and girls and have no record of an annual specialist review in the last 12 month and/or no record of a risk acknowledgement form
- At their next annual specialist review (2024 onwards), women of childbearing potential and girls should be reviewed using a revised valproate Risk Acknowledgement Form, which will include the need for a second specialist signature if the patient is to continue with valproate and subsequent annual reviews (2025 onwards) with one specialist unless the patient's situation changes

### Example codes

## Clinical system coding

	SystemOne code	SNOMED Concept ID
Pregnancy Prevention Programme started <i>To be used when an ARAF is received from secondary care and ongoing annual reviews are required</i>	Y2f16	1129771000000103
Pregnancy Prevention Programme declined <i>To be used the patient has been referred to secondary care, was given an appointment for ARAF completion but did not attend</i>	Y2f17	1129801000000100
Pregnancy Prevention Programme not needed <i>To be used when an ARAF is received from secondary care and ongoing annual reviews are not needed, for example, a patient who is of childbearing age but has had a hysterectomy</i>	Y2f18	1129791000000104
Pregnancy Prevention Programme discontinued	Y2f19	1129841000000102
Did not attend Pregnancy Prevention Programme	Y2f1a	1129831000000106
Pregnancy Prevention Programme declined by parent	Y2f1b	1129821000000109
Pregnancy Prevention Programme declined caregiver	Y2f1c	1129811000000103
Valproate Annual Risk Acknowledgement Form completed <i>To be used when Valproate ARAF received from secondary care</i>	Y362e	1366401000000107
Referral for completion of Valproate Annual Risk Acknowledgement Form <i>To be used when a referral has been made from primary care to secondary care</i>	Y38a6	1366381000000107