PRECONCEPTION GUIDELINES FOR GPs– EPILEPSY

A significant proportion of women affected by epilepsy are of childbearing age. Many of these patients will have well controlled epilepsy and not be in contact with secondary care so primary care has an essential role to play in preconception counselling. There are risks associated with epilepsy and its management in pregnancy, but steps can be taken, especially prior to conception, to help to reduce these risks. Most patients with epilepsy have normal healthy babies and the risk of congenital malformations is low if they are not on any antiepileptic drugs (AEDs) in the preconception period. According to the Royal College of Obstetricians and Gynaecologists, two-thirds of patients with epilepsy will not have seizure deterioration in pregnancy. Pregnant patients who have experienced seizures in the year prior to conception require close monitoring for their epilepsy. Patients should be counselled on the risks of epilepsy during pregnancy.

Risks of epilepsy in pregnancy:

- There are risks associated with taking some AEDs in pregnancy including neural tube defects, congenital heart disorders, urinary tract and skeletal abnormalities and cleft palate. The risk depends on the type, number and dose of AED.
- The information below has been taken from the Medicines and Healthcare products Regulatory Agency (MHRA):
    - Lamotrigine and levetiracetam (brand name Keppra) are safer to use during pregnancy than other epilepsy medicines. Information shows that they do not increase the risk of physical birth abnormalities compared with the general population
    - Carbamazepine, phenobarbital, valproate, phenytoin or topiramate use during pregnancy increases the risk of physical birth abnormalities compared with the general population
    - Phenobarbital or phenytoin taken during pregnancy increases the risk the child may have difficulties with learning and thinking ability. Although the exact risk is not known, it is not as high as for valproate
    - Phenobarbital, topiramate, or zonisamide taken during pregnancy increase the risk of the baby being born smaller than expected compared with the general population
    - Gabapentin and pregabalin – the risks of taking these during pregnancy are not yet fully understood. Some research suggests that taking pregabalin during pregnancy may slightly increase the risk of a baby being born with physical birth abnormalities
    - Zonisamide – more research is needed to understand whether taking zonisamide during pregnancy increases the risk of having a baby being born with a birth abnormality or a learning or thinking disability
    - Clobazam – some research suggests that clobazam may slightly increase the risk of a baby being born with physical birth abnormalities. However, the research that is available does not allow firm conclusions to be reached and the risk of harming a baby cannot be confirmed or ruled out.
- Sustaining an injury during a seizure
- Generalised tonic-clonic (GTC) seizures can lead to fetal hypoxia
- SUDEP (sudden unexplained death in epilepsy)

Preconception advice for patients with epilepsy

- The importance of planning pregnancy should be discussed as well as the increased risk of combined oral contraceptive failure with enzyme-inducing AEDs (such as carbamazepine, oxcarbazepine, phenytoin and topiramate}
- Explain to patients who are planning pregnancy the importance of adherence to their antiseizure medications and that they should **not stop** their medication without specialist medical supervision.
- Patients taking AEDs should have a review by an epilepsy specialist **prior** to conception to minimise exposure to high-risk medications and poly treatment
- The most up to date guidance on AEDs can also be found on the UK teratology information service website (www.uktis.org)
- Discuss that the dose of their medication is likely to need to increase in pregnancy due to haemodilution and weight gain. Blood levels of medication may need to be checked more frequently too.
- Patients considering pregnancy should start **folic acid 5mg** (prescription only dose) at least 3 months prior to conception/trying for a baby until 12/40 gestation if taking AEDs– this should be the case also for all patients taking AEDS for any reason
- Aim for seizure freedom for 2 years before conception and during pregnancy (particularly for those with GTC seizures)
- Give patients verbal and written information on antenatal screening, risks of self-discontinuation of AEDs and status epilepticus/SUDEP (sudden unexplained death in epilepsy), effects of seizures and AEDs on the fetus and pregnancy, breastfeeding and contraception
- Inform patients of safety precautions to reduce risks of accidents and reduce anxiety
- Offer patients **further information** - the MHRA has a very useful document on epilepsy medicines and pregnancy. See www.gov.uk/government/publications/epilepsy-medicines-and-pregnancy. There is also very informative page on the Epilepsy Action Charity Page Titled: “Starting a Family.” https://www.epilepsy.org.uk/living/starting-a-family

Valproate:

- Valproate (e.g. Epilim, Depakote) is associated with a significant risk of birth defects and developmental disorders in children born to patients who take valproate during pregnancy.
- If valproate is taken during pregnancy, up to 4 in 10 babies are at risk of developmental disorders, and approximately 1 in 9 are at risk of birth defects.
- These include spina bifida, facial and skull malformations (including cleft lip and palate) and malformations of the limbs, heart, kidney, urinary tract and sexual organs
- In patients who take valproate while pregnant, about 3–4 children in every 10 may have developmental problems, and these disorders can be seriously debilitating and permanent.

- Valproate must **not** be used in patients of childbearing potential (including young girls who are likely to need treatment into their childbearing years). Since 2018 any use of valproate in patients of childbearing potential must be within the terms of the Pregnancy Prevention Programme. See https://www.gov.uk/guidance/valproate-use-by-women-and-girls
- In September 2024, the MHRA published a Drug Safety Update on valproate use in men and their female partners. For men currently taking valproate
  - as a precaution, recommend that male patients and their female sexual partner use effective contraception (condoms, plus effective contraception used by female sexual partner) throughout the valproate treatment period and for 3 months after stopping valproate, to allow for one completed sperm cycle not exposed to valproate
  - at their next regular treatment review, discuss with men on oral valproate treatment whether they are planning to father a child in the next year and if they are, refer to a specialist to discuss most appropriate treatment options
  - advise men not to donate sperm during valproate treatment and for 3 months after stopping valproate
  - if a female reports they are pregnant or planning a pregnancy with a man on valproate, refer them for prenatal counselling

Topiramate:

- In June 2024, the MHRA published a Drug Safety Update on topiramate as the use of topiramate during pregnancy is associated with significant harm to the unborn child. Harms included a higher risk of congenital malformation, low birth weight and a potential increased risk of intellectual disability, autistic spectrum disorder and attention deficit hyperactivity. Topiramate should not be used in pregnancy for epilepsy unless there is no other suitable treatment. Topiramate should not be used in patients of childbearing potential unless the conditions of the Pregnancy Prevention Programme are fulfilled. See www.gov.uk/drug-safety-update/topiramate-topamax-introduction-of-new-safety-measures-including-a-pregnancy-prevention-programme

If conception occurs whilst on valproate or topiramate then please ensure fetal medicine follow up.

Referral to preconception clinic

There is a preconception clinic at Homerton hospital run by a consultant obstetrician and consultant neurologist. GPs can refer any patient with epilepsy who is planning a pregnancy, and especially if they are:

- Taking AEDs
- Taking valproate or topiramate
- Not seizure free for the past 2 years

How to refer:

- GPs can refer by completing the referral form (available on EMIS and the GP website) and attaching this to an e-RS referral.
- Routine → Obstetrics → maternal medicine

If there are risk factors for inherited forms of epilepsy, then refer for genetic counselling to Ella Hill in Fetal Medicine at **ellahill1@nhs.net**. Risk factors include refractory or difficult to treat epilepsy, other significant neurodevelopmental or neurological symptoms (such as developmental delay, autism spectrum disorder, or movement disorder) or a strong family history of epilepsy.

Any queries, please email the Homerton obstetric query email on **huh-tr.obstetricquery@nhs.net** or neurology advice and guidance on e-RS.

References:

- NICE Epilepsy: Scenario: Contraception, pregnancy, and planning pregnancy
- RCOG Epilepsy in Pregnancy Green-top Guideline No. 68
- MHRA Epilepsy medicines and pregnancy

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