Implementing the Topiramate new safety measures including the Pregnancy Prevention Programme (PPP) in BNSSG

Patient scenario	What can I do to support the MHRA safety recommendations for topiramate?
A **paediatric** patient prescribed topiramate for **epilepsy or migraine** prophylaxis	Patient should be under secondary care as TLS amber 3 months with a shared care protocol currently in place. Therefore, secondary care will undertake the topiramate annual reviews and complete the Annual Risk Awareness Form (ARAF) for the appropriate indication at their next review. Where the child is post menarche ensure they are following the Pregnancy Prevention Programme (PPP). If patient is from out of area or lost to follow up then primary care to refer to appropriate paediatric clinic. If unsure of clinic, please see paediatric advice and guidance on Remedy.
A female **adult epilepsy** patient of childbearing age prescribed topiramate. Topiramate being prescribed by primary care.	GP practice to refer the patient to **the epilepsy team** at **NBT via ERS**. State this is for a 'topiramate review'. Secondary care will review appropriateness of the medication and complete the ARAF, ensuring the patient is adhering to the PPP, if the medication is to continue. Primary care to prescribe ongoing highly effective contraception and continue topiramate prescribing. If a patient is not on contraception, then the GP should discuss with the patient whilst they wait their review. Topiramate is currently 'amber specialist initiated' for epilepsy in the BNSSG Formulary.
A female **adult** patient of childbearing age taking topiramate for **migraine**, prescribed by primary care	Primary care should in the first instance review the patient's topiramate medication: • Is it still required? **If no**: Consider stopping topiramate medication as appropriate. If on contraception, ensure the contraception is continued for 4 weeks after stopping treatment due to topiramate being an enzyme inducing drug[i]. **If yes**: • Are they already using or willing to start highly effective contraception and understand and agree the need to participate in PPP? Then continue, if patient and clinician are happy to do so. GP to complete annual review and complete ARAF. Currently the national recommendation is to continue in primary care. • Alternatively, consider if the patient can have any of the other medications that can be prescribed by primary care e.g. propranolol, candesartan, in the migraine pathway? If yes and patient agrees change the medication. • If the patient isn't happy to commence contraception and the PPP and has tried other options unsuccessfully in the primary

	care part of the migraine pathway refer for advice and/or Anti-CGRP Mab if meets criteria. The prescribing of topiramate in a female of childbearing age without the prescription of contraception/engagement with the PPP would be off-label prescribing for which the prescriber is accountable. Prescribers may therefore wish to stop prescribing the medication for this patient's migraine prophylaxis. Prescribers who choose to continue prescribing should make records of the steps they have taken to manage the risk, the conversation with the patient and that a referral has been made. The waiting time for a non-urgent neurology appointment will need to be considered. The decision to prescribe will need to be on a case by case basis considering individual patient circumstances and indication. Prescribers should consider the good practice guidance from the GMC guidance or GPhC. If you consider there is a compelling reason that there is no potential for pregnancy and the topiramate PPP is not needed, complete "Step 1" on the prophylaxis of migraine ARAF and record clearly in the patient notes. Topiramate is TLS Blue in the BNSSG Formulary for migraine prophylaxis so GP practices can continue ongoing prescribing and completion of annual reviews and ARAF.
A female patient of childbearing age prescribed topiramate for a **non-licensed/non-formulary indications** e.g. tics for Tourette's syndrome or prescribing in pain.	Prescribing for these indications is currently outside of the BNSSG formulary. GP practice should refer patients to the appropriate secondary care team for review of treatment and ongoing monitoring. For mental health conditions - patients to be referred to AWP Service to their usual consultant or via emailing the referral form to PCLS. https://remedy.bnssg.icb.nhs.uk/adults/mental-health/primary-care-liaison-service-awp/ For pain conditions – patients to be referred to their current specialist consultant.
Patient on topiramate who wants to start a family or are pregnant • Epilepsy	**Epilepsy** •The patient should be highlighted to the epilepsy team in secondary care. •Topiramate for epilepsy should **not be stopped abruptly** or without specialist input. Work with local specialist teams as appropriate to the indication.

	•If planning to start a family consider, switching topiramate to another therapeutic option. The conditions of the PPP continue to apply until the switch from topiramate is complete. • Ask the patient not to stop contraception until the switch is achieved and she has no longer taking been taking topiramate for at least a month. • If switching is not possible counselling about the risks. •If an unplanned pregnancy presents, individuals who must continue treatment in pregnancy (i.e. if switching to an alternative treatment is not possible) should be referred for appropriate monitoring.
• Migraine	**Migraine** • Discontinue topiramate in individuals planning a pregnancy. Migraine often improves in pregnancy, typically during the second and third trimesters. Therefore, these individuals do not usually need preventative treatment during pregnancy. • The conditions of the PPP continue to apply until the topiramate has been discontinued. Ask the patient not to stop contraception until she has no longer been taking topiramate for at least a month. • Patients with migraine presenting with an unplanned pregnancy should have their treatment discontinued and liaise with maternity service as needed.
What contraception is recommended for those prescribed topiramate as part of the PPP?	The FSRH recommends at least **one highly effective** method of contraception (copper intrauterine device (Cu-IUD) or levonorgestrel intrauterine system (LNG-IUD) **OR** Depot Provera IM (DMPA) **PLUS** condoms. Please note: As topiramate is a teratogen, the FSRH CEU suggests that it is preferable to err on the side of caution and consider topiramate a potential enzyme inducer, regardless of dose. Therefore, the implant, combined hormonal contraception and progestogen-only pills are not deemed an appropriate option for contraception with topiramate. Emergency contraception: Cu-IUD is the most effective form of emergency contraception and should be offered first line. If a Cu-IUD is not suitable or acceptable, oral emergency contraception should be offered - double dose levonorgestrel (3mg) or standard dose ulipristal acetate (30mg) as indicated. The effectiveness of UPA-EC compared to that of double-dose (3mg) LNG in this situation is unknown. Involve the patient in the discussion about the most appropriate contraceptive method to ensure patient engagement.

	Ensure that the patient understands that even if they have amenorrhoea, they must follow all the advice on highly effective contraception. Consider the possibility of decreased contraceptive efficacy and increased breakthrough bleeding in patients taking systemic hormonal contraceptive products with topiramate. Ask them to report any change in their bleeding patterns; contraceptive efficacy can be decreased even in the absence of breakthrough bleeding. If the patient choses contraception in the form of a copper intrauterine device (Cu-IUD) or levonorgestrel intrauterine system (LNG-IUS) and there is a fitting delay, then ensure the patient is using two forms of contraception including condoms, in the interim whilst on topiramate and awaiting their fitting appointment. Although locally the sexual health clinic Unity may be able to support with the fitting of highly effective contraception, the responsibility for the topiramate annual review should be undertaken by the specialist prescriber or healthcare professional in primary care (depending on the topiramate indication). Any referrals for contraception should be clearly documented in the patient notes.
If the patient is on both topiramate and valproate do they need two separate ARAFs?	Yes, they do and there is a significantly increased risk of teratogenicity with multiple teratogens, so the patient will need an explanation of this and it to be documented in the clinical notes.

[i] Summary of Product Characteristics for Topiramate
https://www.medicines.org.uk/emc/product/1977/smpc

Drug Safety Update, June 24 Topiramate (Topamax): introduction of new safety measures, including a Pregnancy Prevention Programme, https://www.gov.uk/drug-safety-update/topiramate-topamax-introduction-of-new-safety-measures-including-a-pregnancy-prevention-programme

Guide for Healthcare Professionals for Migraine
https://www.medicines.org.uk/emc/rmm/3084/Document

Guide for Healthcare Professionals for Epilepsy
https://www.medicines.org.uk/emc/rmm/3083/Document

Risk Awareness Form for Migraine and Epilepsy

Patient Guide for Migraine and Epilepsy