NHS
Kent and Medway

Topiramate – Implementing MHRA Safety Measures in Kent & Medway

Document History

Title		Topiramate - Implementing MHRA Safety Measures in Kent & Medway
Version	Date	
Draft 1.0	07/08/2024	
Draft 1.1	19/08/2024	Responsibilities in primary and secondary care sections updated following comments received from various stakeholders across sectors.
Draft 1.2	05/11/2024	*Topiramate interaction with Hormonal Contraception* section updated to reflect wording from FSRH CEU guidance.

Document distribution

Version	Clinical committee	Date	Comments
Draft 1.0	IMOSG	14/08/2024	Suggested further engagement

NHS
Kent and Medway

Topiramate – Implementing MHRA Safety Measures in Kent & Medway

June 2024 update:
Topiramate (Topamax): introduction of new safety measures, including a Pregnancy Prevention Programme - GOV.UK (www.gov.uk)

Situation

The use of topiramate is now contraindicated:

- in women of childbearing potential unless the conditions of the Pregnancy Prevention Programme are fulfilled (for all indications)
- in pregnancy for prophylaxis of migraine
- in pregnancy for epilepsy unless there is no other suitable treatment

Background

Topiramate is indicated for epilepsy and migraine prophylaxis (the latter use is unlicensed in children). This regulatory action follows a review by the MHRA which concluded that the use of topiramate during pregnancy is associated with significant harm to the unborn child. For babies of mothers who take topiramate while pregnant the risks are:

- Around 4 to 9 babies in every 100 will have birth defects, this compares with 1 to 3 babies in every 100 born to mothers in the general population.
- A 2 to 3 times higher risk of autism spectrum disorder, attention deficit hyperactivity disorder and intellectual disabilities compared with women without epilepsy not taking epilepsy medicines.
- Around 18 in 100 babies will be born small for gestational age; this compares with around 5 in 100 babies of mothers in the general population.

Action

- Practices should identify all patients of childbearing potential who are being treated with topiramate-containing medicines.
- A record should be kept of these patients, to monitor and facilitate the completion of annual risk awareness forms (ARAF).
- All patients who are prescribed a medication with pregnancy prevention programme requirements should be coded as appropriate with the nationally recognised SNOMED codes. A process should be put in place to ensure these patients are identified and reviewed annually.

SNOMED codes:

Pregnancy prevention programme	1129761000000105
Pregnancy prevention programme started	1129771000000103
Pregnancy prevention programme declined	1129801000000100
Pregnancy prevention programme not needed	1129791000000104
Pregnancy prevention programme discontinued	1129841000000102

Did not attend pregnancy prevention programme	1129831000000106
Pregnancy prevention programme declined by patient	1129821000000109
Pregnancy prevention programme declined caregiver	1129811000000103
Pregnancy prevention programme form signed (verbally agreed) by patient	1960931000006109
Valproate annual risk acknowledgement form completed	1366401000000107
Referral for completion of valproate annual risk acknowledgement form	1366381000000107

Responsibilities – Primary care

Primary Care Guidance Summary- *Please review finer detail below*:

- **For all newly initiated female patients of childbearing potential on Topiramate, it is the initiating clinician's responsibility to complete the Annual Risk Awareness Forms (ARAF)** – *this applies to patients initiated or solely managed in primary care and those initiated by a specialist.*
- **For existing female patients of childbearing potential prescribed Topiramate for migraine prophylaxis, the annual risk awareness forms should be completed within primary care, unless extenuating circumstances would require a specialist review into ongoing treatment.**
- **Patients prescribed topiramate for epilepsy will require referral to neurology specialists for review and annual risk awareness form completion. Full details of the patient's pregnancy prevention plan (including contraception prescribed) should be included when referring to epilepsy specialists for topiramate reviews.**
- **Topiramate Annual Risk Awareness Forms: Migraine and Epilepsy**

For *existing* female patients of childbearing potential on Topiramate, primary care prescribers should:

1. Identify all patients of childbearing potential on topiramate and invite them in for review

2. Complete ARAF with the patient (or responsible person) and at each annual review. Topiramate Annual Risk Awareness Forms: Migraine and Epilepsy.
   - Assess the patient's potential for pregnancy and discuss the need for them to be on the Pregnancy Prevention Programme including highly effective contraception (see contraception section below).

3. Ensure all girls and women of childbearing potential prescribed topiramate are given the new patient guide, for information. ***There are two versions**: epilepsy and migraine prophylaxis. Document (medicines.org.uk) (Migraine) Document (medicines.org.uk) (Epilepsy)

4. Migraine prophylaxis: Undertake annual reviews using the new ARAF for female patients on topiramate for migraine prophylaxis, within primary care.
   - **The MHRA alert states that if a patient thinks they may be pregnant and they are taking topiramate for migraine prevention, they should stop taking topiramate straight away and be switched to an alternative treatment.**

5. Historic patients who have been discharged from a specialist migraine service should have their ongoing reviews in primary care unless circumstances would require a specialist review into ongoing treatment- in which case the patient should be rereferred.

6. Epilepsy: Refer female patients of childbearing potential who are on topiramate for epilepsy and who have an outstanding ARAF to their neurology specialists for completion of a new/ up to date ARAF. Include full details of their current contraception in the referral for topiramate risk awareness review, as applicable.
   - Urgently refer anyone on topiramate who is planning a pregnancy or who is pregnant for specialist advice on their antiepileptic treatment.
   - Patients taking topiramate for epilepsy should NOT stop using the treatment suddenly.

7. The following criteria may be considered as compelling reasons that the reproductive risks do not apply and therefore these patients may be excluded from requiring a pregnancy prevention programme

   Patients may be considered for exclusion if they:

Are over 55 years (unless they are planning a family)
Have had a total or partial hysterectomy
Have had a bi-lateral oophorectomy or bilateral salpingo-oophorectomy (and are not considering IVF)
Have a confirmed menopause or documented no period for 12 months plus
Have been sterilised
Have another documented reason for infertility
Wish to be permanently excluded from the annual review (see point below*)

NOTE:

- Girls who have not yet started menstruating should NOT be excluded.
- *** Patients who have been excluded from the pregnancy prevention programme should still have a final ARAF recorded.**

For all *newly initiated* female patients of childbearing potential on Topiramate primary care prescribers should:

8. Assess the patient's potential for pregnancy and discuss the need for them to be on the Pregnancy Prevention Programme

9. Ensure that pregnancy has been excluded, by means of a negative pregnancy test, prior to starting treatment with topiramate

10. Inform the patient of the potential risks of topiramate use in pregnancy and counsel them on treatment options

11. Discuss the need to use highly effective contraception throughout treatment and for at least four weeks after the last dose of topiramate.

12. Complete the ARAF with the patient (or responsible person) (linked in Point 2 above)

    - It is understood that the majority of Topiramate prescribing in K&M is initiated in primary care for migraine prophylaxis; these patients should continue to be reviewed in primary care.
    - If topiramate has been initiated by a specialist for epilepsy or migraine and/or the patient is still under a specialist service, the GP must ensure they receive a copy of the completed form, and this is coded on the patients record (see specialist responsibilities below).
    - If topiramate has been initiated in primary care at the **recommendation** of a migraine specialist, it is still the initiating clinician in primary care's responsibility to complete the ARAF.

13. Provide a copy of the Patient Guide, for information (linked in Point 3 above)

Responsibilities – Specialists *(For newly initiated and existing service patients)*

- **It is the initiating clinician's responsibility to complete the ARAF** *following points 8-13 above* (**Migraine** **and** **Epilepsy**)
- Review and complete ARAF for patients prescribed topiramate for epilepsy or migraine on initiation
- Recall patients taking topiramate for epilepsy on an annual basis to complete the annual risk awareness form.
- The specialist must send a copy of the signed ARAF either on initiation or on annual review to the GP practice for their records.
- While there are no formally recognised unlicensed indications approved for use in K&M, Topiramate has precedent for being been used off-label at the recommendation of specialists, the need for ongoing treatment should be reviewed by the initiating specialist.

Topiramate interaction with Hormonal Contraception

As well as being a teratogen, at higher doses, topiramate has enzyme-inducing activity. Use of combined hormonal contraception, progestogen-only pills and the etonogestrel implant is **not recommended** as they interact with topiramate and may reduce the effectiveness of these steroidal contraceptives.

The Faculty of Sexual & Reproductive Healthcare (FSRH) CEU suggests that it is preferable to err on the side of caution and consider topiramate a potential enzyme inducer, regardless of dose.

During use of a teratogen that is an enzyme inducer or a potential enzyme inducer (or if an enzyme inducing drug is also being taken) use of the copper IUD, a levonorgestrel-releasing IUS, or depot medroxyprogesterone acetate **PLUS condoms** is recommended.

NHS
Kent and Medway

Use of combined hormonal contraception, progestogen-only pills and the etonogestrel implant (Nexplanon) is not recommended. See FSRH CEU guidance and MHRA guidance:

Clinical Guidance: Drug Interactions with Hormonal Contraception: drug-interactions-with-hormonal-contraception-5may2022.pdf (fsrh.org)

Medicines with teratogenic potential: what is effective contraception and how often is pregnancy testing needed? - GOV.UK (www.gov.uk)