Ref: APCSCG/008
South East London Shared Care Prescribing Guideline for zonisamide for the treatment of epilepsy in ADULTS
Date of original approval: June 2016 **Last reviewed:** August 2020 **Review approved:** October 2020 **Next review date:** October 2022 (or sooner if evidence or practice changes)

SHARED CARE PRESCRIBING GUIDELINE
Zonisamide for the treatment of epilepsy in ADULTS

Zonisamide for the treatment of epilepsy in adults
NOTES to the GP

The information in the shared care guideline has been developed in consultation with NHS South East London Clinical Commissioning Group (CCG) and it has been agreed that it is suitable for shared care.

This document should provide sufficient information to enable you to make an informed decision regarding the clinical and legal responsibility for prescribing **zonisamide** for the treatment of **epilepsy**

The questions below will help you confirm this:

- Is the patient's condition predictable or stable?
- Do you have the relevant knowledge, skills and access to equipment to allow you to monitor treatment as indicated in this shared care prescribing guideline?
- Have you been provided with relevant clinical details including monitoring data?

If you can answer YES to all these questions (after reading this shared care guideline), then it is appropriate for you to accept prescribing responsibility.

If the answer is NO to any of these questions you should contact the requesting consultant or your local Borough Medicines Management Team. There may be implications for the patient where the invitation to share care is declined. For example, the patient may need to be changed to an alternative treatment regimen. It would not normally be expected that shared care prescribing would be declined on the basis of cost.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient by the doctor initiating treatment. **It is important that patients are consulted about treatment and are in agreement with it**.

Prescribing should follow requirements in the South East London Interface Prescribing Policy.
The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use. The patient's best interests are always paramount.

Once you have read the shared care guideline and considered the information above, please complete the GP decision form on the next page and email back to the requesting clinician if you are in agreement to participate in shared care

GP DECISION FORM

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of **zonisamide** for **epilepsy** can be shared between the specialist and general practitioner (GP). GPs are invited to participate. If the GP is not confident to undertake these roles, then he or she is under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable.

AGREEMENT TO PARTICIPATE IN SHARED CARE Zonisamide for treatment of epilepsy in ADULTS	
Consultant/Specialist Name:	**Patient name:**
Consultant/Specialist signature:	**Patient Hospital Number:** **Patient NHS Number:**
Date completed:	**Patient Agreement:**
Hospital requesting shared care:	Patient agrees to shared care ☐ Patient does not agree to shared care ☐
GP Name:	
This is to confirm that I agree to participate in shared care for zonisamide for the treatment of epilepsy for this patient as outlined in this shared care document	
GP Signature:	
Date signed:	

ACTION

1. HOSPITAL CONSULTANT

Tick to confirm

- Explain shared care to patient and obtain agreement Date agreement obtained:_____ ☐
- Indicate requesting hospital ☐
- Complete and sign agreement ☐
- Email full shared care guideline (including signed agreement to GP) ☐
- Place original in patient's notes ☐

2. GP PRACTICE

- If **in agreement** to participate in shared care, sign and email (via secure NHS.net) this sheet back **within 2 weeks** of receipt **of request from specialist** to the email/number on the cover sheet.
- If **do not agree** to participate in shared care, contact consultant and local Medicines Optimisation Team within 2 weeks of receipt to discuss. If after discussion it is agreed not to undertake shared care for this patient, both the consultant and the local Medicines Optimisation Team should be informed.
- Once decision reached file a copy in the Patient's medical notes.

Zonisamide 25mg, 50mg and 100mg Capsules for the treatment of Epilepsy in Adults

Zonisamide is indicated as monotherapy and adjunctive therapy in the treatment of adult patients with partial seizures, with or without secondary generalisation. It is expected that zonisamide will be prescribed as an adjunct to other anti-epileptic drugs, in the management of partial onset seizures which have not responded to monotherapy. (For more details on place in therapy see: South East London Integrated Medicines Optimisation Committee (formerly Area Prescribing Committee) Anti-epileptic Drug Treatment Pathway for Focal Epilepsy in adults.

CIRCUMSTANCES WHEN SHARED CARE IS APPROPRIATE

- Prescribing responsibility will only be transferred when the consultant and the GP are in agreement that the patient's condition is stable or predictable.
- The hospital will provide the patient with **two** month's supply of therapy

2. AREAS OF RESPONSIBILITY

Consultant / Specialist team responsibilities

- Ensuring patient fits criteria for use of this drug (e.g. no contraindications, cautions, fits local agreement for use of the drug)
- Baseline monitoring tests:
  Full blood count and biochemistry including bicarbonate undertaken in secondary care on initiation.
- To initiate, stabilise and supply treatment over the first **two months**
- To provide a clinic letter clearly detailing individualised titration regimen which will be discussed in detail with the patient. This will include clear documentation of dose increments, parameters to be met before dose change is made, and when dose titration should stop.
- To inform patients of practical issues related to the use of zonisamide, such as administration, storage and maximum dose – see "Information provided to patient" section on page 5 and 6
- At the time of initiating, notify GP in writing that zonisamide has been prescribed. The GP should be invited to share care once the patient is stable. Information provided to the GP should include:
  - A copy of the shared care guidelines
  - That a prescription for the first **two months'** supply has been given
  - Information on when the patient will next be reviewed and by whom.
  - A request that the GP continue prescribing after **two months**.
- Any continuous monitoring that will remain under the consultant's responsibility
- To review patient at the request of GP should any problems arise (side-effects / lack of efficacy).
- To communicate promptly with the GP if treatment is changed.
  To report any suspected adverse effects to the MHRA: https://yellowcard.mhra.gov.uk/

General Practitioner responsibilities

- To consider shared care proposal within 2 weeks of receipt. If agree to request to continue prescribing as detailed in shared care guideline. Confirmation to the requesting consultant is required **within 2 weeks** of receipt of this guideline by completing and returning the agreement on page 2
- If do not agree to shared care discuss with requesting consultant or local primary care Medicines Optimisation Team within 2 weeks of receipt of shared care request
- To provide ongoing prescriptions for zonisamide after **2 months**
- To adjust the dose as advised by the specialist.
- To agree monitoring requirements with specialist – see page 5 of this document for GP monitoring requirements.

- To report and seek advice regarding any concerns, for example: side-effects, co-morbidities, pregnancy, or lack of efficacy to the specialist team
- To advise the specialist if non-compliance is suspected
- To refer back to specialist if the patient's condition deteriorates.
- Check compatibility interactions when prescribing new or stopping existing medication
- To stop treatment on the advice of the specialist or immediately if an urgent need to stop treatment arises.
- Discuss any abnormal results with specialist consultant and agree any action required
- Only ask specialist to take back prescribing should unmanageable problems arise. Allow an adequate notice period.
- Add details of zonisamide prescription on to patients Patient Medical Records at GP practice
- Continue to act as primary contact for general healthcare
- To report any suspected adverse effects to the MHRA via the Yellow Card scheme: https://yellowcard.mhra.gov.uk/.

Patient's / Carer's responsibilities
▪ To contact the specialist or GP if he or she does not have a clear understanding of any aspect of the treatment. ▪ To inform prescribing specialist, GP and other healthcare professionals of any other medication being taken, including over the counter products, alternative therapies or recreational drugs. ▪ To inform community pharmacists that they are using zonisamide before purchasing medication over-the-counter ▪ To attend all hospital and GP appointments ▪ To take medicines as agreed and take steps to ensure that no doses are missed and not to share medicines with others ▪ To read the patient information leaflet included with the medication. ▪ To report any adverse effects or warning symptoms to GP or hospital specialist ▪ To report to GP and epilepsy team if pregnant or breastfeeding. ▪ To inform GP and hospital of any changes in addresses or telephone contact numbers.

3. CLINICAL INFORMATION

NOTE: The information here is not exhaustive. Please also consult the current Summary of Product Characteristics (SPC) for **zonisamide** prior to prescribing for up to date prescribing information, including detailed information on adverse effects, drug interactions, cautions and contraindications (available via www.medicines.org.uk)

Indication(s)
Adjunctive therapy in the treatment of adult patients with partial seizures, with or without secondary generalisation.
Place in Therapy
It is expected that zonisamide will be prescribed as an adjunct to other antiepileptic drugs, in the management of partial onset seizures which have not responded to monotherapy
Dose & route of administration
For most patients, initially 50mg daily in 2 divided doses. Half-life is long and it takes about 13 days to reach a steady state. Dose increases are guided by clinical state, response and tolerability. Usual maintenance 300-500mg daily in 1-2 divided doses
Duration of treatment
Long term, pending clinical response
Criteria for stopping treatment
Significant side effects, lack of response at adequate/tolerated doses

Monitoring Requirements including frequency

Consultant:

Baseline: weight, full blood count and biochemistry including bicarbonate.
Ongoing (in specialist clinic): seizure charts, weight, side-effects, repeat full blood count and biochemistry including bicarbonate where indicated.

GP:

No routine blood tests however, GP may be specifically requested to help with blood test monitoring where more convenient/appropriate for patient. If GP is required to do blood tests, the tests required will be clearly indicated in the clinic letter, and results should be communicated back to the consultant. They are likely to include full blood count and biochemistry (including bicarbonate). Follow up and monitoring of dose adjustments e.g. side effects/tolerance within guidance in clinic letter.

- To report any concerns about side-effects (possible allergic reactions, excessive somnolence, dizziness), co-morbidities (seizures, severe cardiovascular disease, mental illness), pregnancy, overuse or lack of efficacy to the epilepsy specialist team (Specialist nurse or consultant)
- Report any suspected adverse effects to the MHRA: https://yellowcard.mhra.gov.uk/.

Follow up arrangements

Consultant: Follow up in specialist clinic 3-6 monthly. There is an option of urgent access to an earlier appointment or telephone or email advice in between scheduled appointments. This is usually coordinated through the specialist nurse. An initial **two months** (**56 days**) supply will be made at the outpatient clinic appointment. The clinic letter will clearly detail an individualised titration regimen which will be discussed with the patient in detail. This will include clear documentation of dose increments, parameters to be met before dose change is made, and when dose titration should stop.

GP: Patient will be advised to see GP within 4 weeks of consultant initiation to verify compliance and organise further supplies. A specific individualised dose titration regime will be provided in the clinic letter. The GP is NOT expected to titrate the dose outside the individualised guidance and parameters detailed in the clinic letter and if deviation from guidance on dose titration is required this should be discussed with the secondary care team.

The GP should review patients at a minimum of annually as part of standard epilepsy care.

Practical issues including other relevant advice/information

Reminder: this list is not exhaustive - for full details of adverse effects and all potential drug interactions refer to latest Summary of Product Characteristics (SPC) for the drug, available via www.medicines.org.uk.

For general information and full details of contraindications, precautions, drug interactions and adverse effects of zonisamide please see the summary of product characteristics (SPC) available at www.medicines.org.uk

Prior to initiation of zonisamide the following will be excluded by the consultant: A personal or close family history of kidney stones, a history of sulphonamide hypersensitivity and severe liver impairment.

All patients initiated on zonisamide will be advised by the consultant:

- Of the possibility of somnolence/dizziness/anorexia/allergies/skin/rash/mouth ulcers
- To ensure they remain well hydrated to minimise the risk of kidney stones.
- That the risk in pregnancy is unknown (for women of child bearing age)
- Suicidal ideation and behaviour have been reported in patients treated with anti-epileptic agents in several indications. Patients (and caregivers of patients) will be advised to seek medical advice should signs of suicidal ideation or behaviour emerge.

The clinical response and patient factors e.g. concomitant therapy with CYP3A4 inducing agents (refer to page 2 of the SEL AED Pathway for examples), and renal or hepatic impairment will be taken into account by the consultant in relation to the detailed dose escalation provided. For information it should be noted that higher doses are not always associated with a better response, and may precipitate more side effects.

Serious rashes can occur in association with zonisamide therapy including cases of Stevens – Johnson syndrome. If a GP suspects that zonisamide may be the cause of a rash then immediate contact should be made with the secondary care team for further advice.

Discontinuation of zonisamide will usually be directed by the secondary care team including detailing a staged dose reduction. If a GP believes that discontinuation is appropriate for any reason then advice should be sought immediately from the secondary care team.

In patients taking zonisamide who develop the clinical signs and symptoms of pancreatitis, lipase and amylase levels should be taken by the clinician who diagnoses the signs (Consultant or GP). If pancreatitis is evident in the absence of another obvious cause, appropriate treatment must be initiated and the need for continued therapy must be immediately discussed with the secondary care team.

If acute renal failure or a clinically significant sustained increase in creatinine is observed by the GP then immediate referral to the secondary care team should be made for further advice. Any concerns with rising creatinine should be referred to the specialist team. If worsening renal function is identified by the consultant during routine monitoring then a review of zonisamide therapy will be undertaken by the consultant and the outcome will be communicated to the GP.

If muscle pain and/or weakness develop either in the presence or absence of a fever, it is recommended that markers of muscle damage are assessed including serum creatine phosphokinase and aldolase levels and referral is made to secondary care consultant.

A syndrome of myopia and secondary angle glaucoma has been reported with zonisamide. Symptoms include acute onset of decreased visual acuity and/or ocular pain. Caution should be used when treating a patient with a history of eye disorders with zonisamide.

Metabolic acidosis is associated with zonisamide treatment (caused by renal bicarbonate loss due to the inhibitory effect of zonisamide on carbonic anhydrase) and therefore any drop in measured bicarbonate should be immediately reported to the secondary care team. Conditions or therapies that predispose to acidosis may be additive to the bicarbonate lowering effects of zonisamide.

Cases of decreased sweating and elevated body temperature have been reported mainly in paediatric patients. Caution should be used in adults when patients are treated concomitantly with other medicinal products which might predispose to heat related disorders for example carbonic anhydrase inhibitors and medicinal products with anticholinergic activity.

Zonisamide may cause weight loss. A dietary supplement or increased food intake may be considered if the patient is losing weight or is underweight whilst on this medication. If substantial undesirable weight loss occurs, discontinuation of Zonisamide should be considered. For example if a patient lost weight which led to a change in BMI to underweight they should be referred to secondary care for review.

For full details of all other adverse effects refer to the latest version of the SPC

http://www.medicines.org.uk/emc/medicine/16240/SPC/Zonegran+25%2c+50%2c+100+mg+Hard+Capsules/

Zonisamide is not considered to be a narrow therapeutic index drug, however, as with all anti-epileptic medications, it is recommended that supply is maintained with a particular manufacturer unless the prescriber, in consultation with the adult and their family and/or carers as appropriate considers that this is not a concern.[2]

Information provided to the patient

A clinic letter containing details of an individualised dose titration regime will also be provided. This will include clear documentation of dose increments, parameters to be met before dose change is made, and when dose titration should stop.

Evidence Base for treatment and key references

1. Web page: NHS Choices Website: www.nhs.uk/ServiceDirectories/Pages/ServiceSearch.aspx
2. Summary of Product Characteristics- Zonegran – www.medicines.org.uk accessed 16/07/2020 (SPC last updated 26/05/2020)
3. National Institute for Health and Clinical Excellence (2012) The Epilepsies: the diagnosis and management of the epilepsies in adults and children in primary and secondary care. Department of Health, London.
4. South East London Integrated Medicines Optimisation Committee (formerly the SEL APC); Anti-epileptic Drug Treatment Pathway for Focal Epilepsy in adults; Last updated August 2020

4. COMMUNICATION AND SUPPORT

King's College and Princess Royal Hospitals switchboard: 0203 299 9000	
Consultant/specialist team Dr Robert Elwes Dr Lina Nashef Dr Delamont Dr J Quirk Dr L Mantoan Dr R Singh CNS Cathy Queally CNS Debbie Miller	Tel: 02032999000 ext 38331
Medication – Prescribing advice, interactions, availability of medicines Deborah Clark (Clinical Pharmacy Team leader, Neurosciences) Vanessa Eustace (Advanced Senior Clinical Pharmacist, Neurosciences Shelley Jones (Consultant Pharmacist, Neurosciences)	Tel: 0203299900 ext 35717 Email: kch-tr.neuropharmacy@nhs.net

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