Eslicarbazepine (Zebinix®) (Amber with Shared Care)

For the adjuvant treatment of partial onset seizures with or without secondary generalisation in patients over 18 years of age

Shared Care Guidelines: For use in Neurology

AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

This shared care agreement outlines how responsibility for the prescribing of eslicarbazepine for epileptic seizures might be shared between 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.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care is usually explained to the patient by the doctor initiating treatment. It is important that patients are consulted about treatment and are in agreement with it. Patients with epilepsy are usually under regular specialist follow-up, which provides an opportunity to discuss drug therapy.

The doctor who prescribes this medication legally assumes clinical responsibility for the drug and the consequences of its use.

RESPONSIBILITIES and ROLES

	Specialist responsibilities
1	Confirm the diagnosis of epilepsy.
2	Confirm that the patient's epilepsy has failed to be controlled on all other relevant / tolerated anti-epileptic drugs at optimal doses, or that the patient has a very specific reason for requiring a once-daily dosing regimen (e.g. non-resident carer administration).
3	Perform all relevant baseline assessments and periodically review the patient's renal and hepatic function (as necessary for the individual patient).
4	Discuss the benefits, side-effects and possible drug interactions of eslicarbazepine with the patient, including information on its effect on driving if the patient is eligible to drive.
5	Ensure the compatibility of any concomitant medication with eslicarbazapine.
6	Discuss the shared care arrangement with the patient & obtain their consent.
7	Ask the GP whether he or she is willing to participate in shared care before initiating treatment, so that appropriate arrangements can be put in place for follow-on prescribing.
8	Initiate treatment and retain prescribing responsibility for at least 1 month or until the patient is stabilised on a maintenance dose of eslicarbazepine, whichever is the longer, before transferring prescribing responsibility to the patient's GP.
9	Continue to prescribe after the patient is stabilised on a maintenance dose of eslicarbazepine until the GP confirms (s)he is happy to share care.
10	Review the patient's condition and monitor response to treatment at least annually or where deemed clinically necessary. If the patient remains seizure-free then, as long as there is a channel of communication between specialist and GP, the specialist does not need to see the patient again.
11	Provide the GP with a written summary of all hospital out-patient reviews or in-patient stays, within 10 working days.
12	Respond promptly when asked to review the patient and their therapy.
13	Give advice to the GP on when to stop treatment.
14	Report any significant or previously unknown adverse events to the GP and the MHRA via the yellow card reporting scheme https://www.gov.uk/report-problem-medicine-medical-device.
15	Ensure that clear backup arrangements exist for GPs to obtain advice and support should they need it.

	General Practitioner responsibilities
1	Reply to the request for shared care as soon as practicable i.e. within 10 working days.
2	Be satisfied the patient has tried and failed on all other relevant / tolerated anti-epileptic drugs at optimal doses, or that the patient has a very specific reason for requiring a once-daily dosing regimen (e.g. non-resident carer administration).
3	Assume responsibility for prescribing eslicarbazepine after the initial 1 month of treatment under specialist care, provided the patient has been stabilised on a maintenance dose by then.
4	Prescribe eslicarbazepine at the dose recommended.
5	Ensure compatibility of eslicarbazepine with other concomitant medication.

This ESCA should be read in conjunction with the Summary of Product Characteristics (SPC) http://www.medicines.org.uk/emc/medicine/22376
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6	In the patient's notes, using the appropriate Read Code listed below, document that the patient is receiving treatment under shared care agreement:

GP prescribing system	Read code	Description	GP prescribing system	Read code	Description
EMIS and Vision	8BM5.00	Shared care prescribing	System One	XaB58	Shared Care

7	Monitor the patient's response to treatment; make dose adjustments as agreed with specialist.
8	Report to, and seek advice from, the specialist or clinical nurse specialist if the condition deteriorates, or if any aspect of patient care is of concern to the GP, patient or carer and may affect treatment.
9	Report any significant or previously unknown adverse events to the specialist and MHRA via the yellow card reporting scheme https://www.gov.uk/report-problem-medicine-medical-device.
10	Stop treatment, or initiate its tapered withdrawal, on the advice of the specialist.

Patient responsibilities	
1	Attend all appointments with GP and specialist including appointments for blood tests and monitoring.
2	Report to the specialist, clinical nurse specialist or GP if he or she does not have a clear understanding of the treatment.
3	Share any concerns in relation to treatment with eslicarbazepine with the specialist, clinical nurse specialist or GP.
4	Inform the specialist, clinical nurse specialist or GP of any other medication taken, including over-the-counter, herbal and homeopathic products.
5	Report any adverse effects (e.g. mood swings) to the specialist or GP whilst taking eslicarbazepine.

BACK-UP ADVICE AND SUPPORT

Name	Designation	Email address	Telephone No.
Sarah Davis	Epilepsy Nurse Specialist (RUH)	Sarah.davis22@nhs.net	01225 825856
Nicola Giffin	Consultant neurologist	nicola.giffin@nhs.net	01225 825456

SUPPORTING INFORMATION

Background
20-30% of patients with partial epilepsy will either fail to sustain their remission despite optimal doses of anti-epileptic drugs (AEDs) or will suffer significant adverse effects from their AEDs. Several new AEDs have been developed to try to improve this picture, and, in the UK, eslicarbazepine acetate is available as an adjunctive therapy, particularly for those currently on non-sodium channel AEDs.

Indication
Eslicarbazepine is indicated as an adjunctive therapy for the treatment of partial onset seizures, with or without secondary generalisation, in patients over 18 years of age, and it is licensed for this indication.

Dosage and administration
Eslicarbazepine should be added to existing anticonvulsant therapy and titrated on the basis of clinical effect. The recommended starting dose is 400mg once daily, increased to 800mg once daily after one to two weeks. Based on individual response, the dose may be increased to 1200mg once daily.

Renal impairment
- **Mild** (eGFR>60ml/min): No dose adjustment necessary
- **Moderate** (eGFR 30-60ml/min): Reduce initial dose to 400mg every other day for 2 weeks, then increase to 400mg once daily with potential to cautiously increase further based on individual response.
- **Severe** (eGFR<30ml/min): Use is not recommended.

Hepatic impairment
- **Mild to moderate**: No dose adjustment necessary.
- **Severe**: Use is not recommended.

Contra-indications
- Hypersensitivity to eslicarbazepine acetate, to other carboxamide derivatives (e.g. carbamazepine, oxcarbazepine) or to any of the excipients.
- Known second or third degree atrioventricular (AV) block.

Cautions

- Eslicarbazepine acetate has been associated with some central nervous system adverse reactions, such as dizziness and somnolence, which could increase the occurrence of accidental injury.
- Rash developed as an adverse reaction in 1.1% of patients treated with eslicarbazepine acetate in placebo-controlled add-on studies in epileptic patients. If signs or symptoms of hypersensitivity develop, eslicarbazepine acetate must be discontinued.
- Patients who are positive for the HLAB*1502 allele may be at risk for developing Stevens Johnson syndrome (SJS) after treatment with eslicarbazepine acetate. The prevalence of HLA-B*1502 carrier is about 10% in Han Chinese and Thai populations. These individuals should be screened for this allele before starting treatment.
- Hyponatraemia has been reported as an adverse reaction in 1.2% of patients treated with eslicarbazepine acetate. Frequency of hyponatraemia increases with increasing eslicarbazepine acetate dose. In patients with pre-existing renal disease leading to hyponatraemia or in patients concomitantly treated with medicinal products which may themselves lead to hyponatraemia, serum sodium levels should be examined before and during treatment with eslicarbazepine acetate. Serum sodium levels should also be determined if clinical signs of hyponatraemia occur. If clinically relevant hyponatraemia develops, eslicarbazepine acetate should be discontinued.
- Prolonged PR intervals have been observed in clinical studies with eslicarbazepine acetate. Caution should be exercised in patients with medical conditions or when taking concomitant medicinal products known to be associated with PR prolongation.
- Patients should be monitored for signs of suicidal ideation and behaviours and appropriate treatment considered.

Please refer to the SPC http://www.medicines.org.uk for further information on contra-indications, warnings and precautions for use.

Drug Interactions

Carbamazepine	plasma concentration of eslicarbazepine possibly reduced by carbamazepine but risk of side-effects increased.
Fosphenytoin	plasma concentration of eslicarbazepine reduced by fosphenytoin , also plasma concentration of fosphenytoin increased.
Oestrogens	eslicarbazepine accelerates metabolism of oestrogens (reduced contraceptive effect with combined oral contraceptives, contraceptive patches, and vaginal rings—see Contraceptive Interactions in SPC).
Oxcarbazepine	manufacturer of eslicarbazepine advises to avoid concomitant use with oxcarbazepine
Phenytoin	plasma concentration of eslicarbazepine reduced by phenytoin, also plasma concentration of phenytoin increased.
Progestogens	eslicarbazepine accelerates metabolism of progestogens (reduced contraceptive effect with combined oral contraceptives, progestogen-only oral contraceptives, contraceptive patches, vaginal rings, etonogestrel-releasing implant, and emergency hormonal contraception—see Contraceptive Interactions in SPC).
Rosuvastatin	eslicarbazepine reduces plasma concentration of rosuvastatin.
Simvastatin	eslicarbazepine reduces plasma concentration of simvastatin —consider increasing dose of simvastatin.
Warfarin	eslicarbazepine reduces plasma concentration of warfarin.

Please note shaded sections indicate particularly significant interactions; please see current SPC http://www.medicines.org.uk for more details.

Side-effects

As with other medicines, side-effects of eslicarbazepine are classified as very common (≥ 1/10), common (≥ 1/100 to <1/10), uncommon (≥ 1/1,000 to <1/100), rare (≥ 1/10,000 to <1/1000) and very rare (<1/10,000).

Very common

Dizziness & somnolence

Common
Hyponatraemia, decreased appetite, insomnia, headache, disturbance in attention, tremor, ataxia, balance disorder, diplopia, blurred vision, vertigo, nausea, vomiting, diarrhoea, rash, fatigue, gait disturbance, and asthenia

Refer to the SPC for a full list of adverse effects & further information http://www.medicines.org.uk. Seek advice from the specialist if any of these side-effects cause concern.

This medicine does not have black triangle (▼) status, but all serious suspected reactions (even if well recognised or causal link uncertain) should still be reported to the MHRA via their yellow card reporting scheme https://www.gov.uk/report-problem-medicine-medical-device.

Monitoring
- THE GP IS NOT REQUIRED TO UNDERTAKE ANY ROUTINE BIOCHEMICAL MONITORING.
- Baseline assessment of renal and hepatic function by the specialist will guide initial dosing.
- Adhoc review of renal and hepatic function by the specialist/GP will guide dose adjustment.
- Where the GP incidentally finds renal and hepatic function to be abnormal and likely to warrant dose adjustment, advice on dose adjustment should be sought from the specialist as soon as possible.
- The GP is asked to assess serum sodium levels if clinically indicated (see under 'hyponatraemia' in 'Cautions' above), and to seek advice from the specialist if clinically relevant hyponatraemia develops.
- The GP is asked to monitor seizure control and refer to the specialist if seizure control is unsatisfactory.
- The GP is asked to monitor for suicidal ideation, suicidal behaviour and any other adverse effects, and to seek advice from the specialist should they occur.

Storage
Eslicarbazepine acetate does not require any special storage conditions.

Cost
30 Eslicarbazepine acetate 800mg tablets= £136.00 (excl. vat) (BNF August 2017)

References

1. Eisai Ltd. (2017). *Summary of Product Characteristics (Zebinix)* [online]. Hatfield: Eisai Ltd. Available from http://www.medicines.org.uk/emc/medicine/22376. [Accessed on 22nd August 2017].
2. National Institute for Health and Care Excellence (2016). *Epilepsies: diagnoses and management. Clinical Guideline 137* [online]. London: National Institute for Health and Care Excellence. Available from https://www.nice.org.uk/guidance/cg137. [Accessed 22nd August 2017].
3. Birmingham, Sandwell, Solihull and environs (BSSE) Area Prescribing Committee (2015). *Effective shared care agreement - Eslicarbazepine acetate* [online]. Birmingham: BSSE Area prescribing Committee. Available from: http://www.birminghamandsurroundsformulary.nhs.uk/docs/ESCA/BSSE%20APC%20ESCA%20Eslicarbazepine%20acetate%20-%20FINAL%20Sept%2015.pdf?uid=46938673&uid2=201592215175595&UNLID=487354353201682313 4937&UNLID=63165634820179414936 [Accessed 22nd August 2017].

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