City and Hackney Clinical Commissioning Group
Homerton University Hospital Foundation Trust

SHARED CARE GUIDELINE

OXCARBAZEPINE

Treatment of epilepsy in adults and children ≥6 years

DOCUMENT TO BE SCANNED INTO ELECTRONIC RECORDS AND FILED IN NOTES

INTRODUCTION – Indication and Licensing

The pharmacological activity of oxcarbazepine is primarily exerted through the metabolite 10-monohydroxy derivative (MHD). The metabolite MHD exerts its anticonvulsant effect mainly by blocking voltage-sensitive sodium channels, and in addition, by increased potassium conductance and modulation of high-voltage activated calcium channels.

Oxcarbazepine is licensed as monotherapy or adjunctive therapy for the treatment of partial (focal) seizures with or without secondarily generalised tonic-clonic seizures.

PATIENT PATHWAY

Clinical Speciality / Indication	**Prescribing Initiated by**	**Prescribing Continued by** ***(detail when suitable for transfer to occur)***	**Monitored by** ***(detail when suitable for transfer to occur IF APPROPRIATE)***	**Duration of treatment**
Neurology/ Epilepsy	Epilepsy Specialist	GP to take over after 2 months or after the patient has been titrated to a stable therapeutic dose.	Effect on seizure control monitored by hospital and GP.	Indefinite if treatment tolerated and effective.

Reviews & dosing adjustments

- The patient will be followed up by the epilepsy specialist team at the hospital for review of treatment efficacy and tolerability. The patient will be given contact details for the team.
- Dosing adjustments are to be undertaken by the hospital and this information communicated to the GP in writing within 14 days.
- Correspondences from GP should be addressed to the 'Consultant Epileptologist' and NOT to neurology.

ORAL DOSE AND ADMINISTRATION

	Initial	**Titration**	**Maximum dose**
Standard dosing in adults	300mg twice daily	Increase in steps of up to 600mg/day at weekly intervals according to response and tolerability. *Usual maintenance dose:* 600 – 2400mg/day in divided doses. Note in adjunctive therapy, the dose of concomitant antiepileptics may need to be reduced when using high doses of oxcarbazepine.	2400mg/day in divided doses
Standard dosing in children (6-18 years)	8 – 10mg/kg/ day in 2 divided doses	Increase in steps of up to 10mg/kg/day at weekly intervals according to response and tolerability. *Usual maintenance dose:* 30-46mg/kg/day in divided doses. **See the summary of product characteristics for more information on drug clearance in children.**	46mg/kg/day in divided doses
Hepatic impairment	*Mild or moderate* – no dosing adjustment required.		
Renal impairment	*CrCl ≥30ml/min* – no dosing adjustment required. *CrCl <30ml/min* – initiate at half the usual starting dose (300mg/day) and increase at weekly intervals according to response and tolerability with careful observation. **See the summary of product characteristics for more information.**		
Patients ≥65 years	No dosing adjustment required.		

Other considerations:

- May be taken with or without food.
- The tablets are scored and can be broken into two halves in order to make it easier for the patient to swallow the tablet. The tablet cannot be divided into equal doses, **use oral suspension for accurate dosing** and the prescribed dose in millilitres should be rounded to the nearest 0.5 ml.
- **Switching between different manufacturers** – (MHRA category 2) the need for continued supply of a particular manufacturer's product by brand should be based on clinical judgement and consultation with the patient or their carer, taking into account factors such as seizure frequency and treatment history. Note dose conversion is not required when changing between oxcarbazepine tablets and liquids.
- **Potential childbearing age –** discuss with the epilepsy specialist team regarding the benefits of treatment, risks in pregnancy and contraceptive advice. All women with epilepsy should be advised to take 5 mg daily of folic acid prior to conception and to continue taking this until at least the end of the first trimester to reduce the incidence of major congenital malformation.
- **Driving** – advise the patient to inform the Driver and Vehicle Licensing Agency (DVLA) about their epilepsy. See the Epilepsy Action website for more information.

CAUTIONS

- **Hypersensitivity to Carbamazepine** – approximately 25-30 % of these patients may experience hypersensitivity reactions to oxcarbazepine.
- **Suicidal ideation and behaviour** have been reported in patients treated with anti-epileptic medicinal products in several indications. The available data do not exclude the possibility of an increased risk for oxcarbazepine.
- **Severe hepatic impairment** – no information available.

CONTRAINDICATIONS

- Acute porphyria

INTERACTIONS

- **CYP3A4 and CYP3A5** – oxcarbazepine and its pharmacologically active metabolite MHD are weak inducers. See the BNF and summary of product characteristics for more information on drug interactions.
- **Hormonal contraceptives** – oxcarbazepine accelerates metabolism of oestrogens and progestogens. Additional non-hormonal forms of contraception are recommended when using oxcarbazepine.
- **Alcohol** – additive sedative effect.
- **Anticonvulsant effect of antiepileptics reduced by**: selective serotonin reuptake inhibitors, tricyclic (and related) antidepressants, monoamine oxidase inhibitors, antipsychotics, mefloquine and orlistat.

MONITORING STANDARDS FOR MEDICATION AT THE ACUTE NHS TRUST

HLA-B*1502 allele testing	HLA-B*1502 carrier is about 10% in the Han Chinese and Thai populations and these individuals are at high risk of developing Stevens-Johnson syndrome (severe cutaneous reactions). AVOID oxcarbazepine if positive (unless no alternative).
Sodium	Monitor plasma-sodium concentration in patients at risk of hyponatraemia.
Weight	Patients with cardiac insufficiency and secondary heart failure should have regular weight measurements to determine occurrence of fluid retention.
Thyroid function	Thyroid function monitoring is recommended in the paediatric age group while on treatment with oxcarbazepine.
MHD Plasma levels	Monitoring of the plasma levels may be useful in certain situations, including: changes in renal function, pregnancy and concomitant use of liver enzyme-inducing drugs. This will be done by the specialist team.

Seizure diary

- The patient will be given a seizure recording diary, which they will be encouraged to use for the first 6 months of therapy. The patient will be able to record in the diary the nature of the seizure and frequency, and any side effects or problems that they experienced with the treatment.

- A pdf copy of the seizure diary and the Epilepsy Toolkit smartphone app can be downloaded from the Epilepsy Society website (see page 5).

KEY ADVERSE EFFECTS & ACTIONS

Adverse effects	**Symptoms/signs** *(specify what would prompt action)*	**Actions (***what action should the GP take if identified in primary care)*
Hypersensitivity and serious dermatological reactions	Rash, pruritus, urticaria, angioedema and anaphylaxis. **Stevens-Johnson syndrome and toxic epidermal necrolysis (Lyell's syndrome)** - sore throat, fever, chills, and other signs of infection, joint pain or swelling, muscle pain, red, itchy rash, facial swelling and swollen lips covered in crusty sores, ulcers and blisters.	**Stop medication and seek urgent advice** from the specialist team. Serious reactions may require hospitalisation.
Haematological disorders	Agranulocytosis, aplastic anaemia and pancytopenia.	**Seek advice** from the specialist team and **stop medication if severe.**
Central nervous system effects	Somnolence, dizziness and headache. Very common ≥10%	Advise patient not to drive a vehicle, operate complex machinery or engage in other potentially hazardous activities. **Reduce dose if severe** after discussion with the specialist team.
Eye disorders	Double vision (very common ≥10%), blurred vision and visual disturbances.	**Reduce dose if severe** after discussion with the specialist team.
Nausea, vomiting and fatigue	Very common ≥10%	**Reduce dose if severe** after discussion with the specialist team.
Hepatobiliary disorders	Liver impairment and abnormal liver function tests. AST/ALT >2 times upper limit of normal	Check for concomitant drugs that are known to raise liver enzymes. **Seek advice** from the specialist team. **Reduce dose or stop** (depending on severity).
Electrolyte disturbances	Hyponatraemia Sodium <125mmol/l	**Reduce dose or stop** (depending on severity) after discussion with the specialist team.

***Patients and their carers should be told how to recognise signs of blood, liver, or skin disorders, and advised to seek immediate medical attention if symptoms such as lethargy, confusion, muscular twitching, fever, rash, blistering, mouth ulcers, bruising, or bleeding develop.**
***Patients should be monitored for signs of suicidal ideation and behaviours and appropriate treatment should be considered. Patients and their carer should be advised to seek medical advice should signs of suicidal ideation or behaviour emerge.**

The SCG lists only the key information. Please refer to the current British National Formulary and Summary of Product Characteristics for comprehensive information on cautions, contraindications, interactions and adverse effects.

PREGNANCY AND BREAST FEEDING

- **Pregnancy** – there is no increase in the total rate of malformations with oxcarbazepine as compared with the rate observed in the general population (2-3%). However, a moderate teratogenic risk cannot be completely excluded due to the limited amount of data. Minimum effective doses should be given, and monotherapy whenever possible should be preferred at least during the first three months of pregnancy. The specialist team will discuss options with the patient. All pregnant women with epilepsy, whether taking medication or not, should be encouraged to **notify the UK Epilepsy and Pregnancy Register** (Tel: 0800 389 1248).
- **Newborn child** – bleeding disorders in the newborn have been reported with hepatic enzyme-inducing antiepileptic drugs. As a precaution, vitamin K should be administered as a preventive measure in the last few weeks of pregnancy and to the newborn.

- **Breastfeeding** – oxcarbazepine and its active metabolite (MHD) are excreted in human breast milk. The specialist team will discuss this with the patient.
- **Fertility** – there are no human data on fertility. In rats, oxcarbazepine had no effects on fertility. Effects on reproductive parameters in female rats were observed for MHD at doses comparable to those in humans.

For comprehensive information please refer to the current British National Formulary and Summary of Product Characteristics.

SHARED CARE

Shared care guideline*:* is a document which provides information allowing patients to be managed safely by primary care, secondary care and across the interface. It assumes a partnership and an agreement between a hospital specialist, GP and the patient and also sets out responsibilities for each party. The intention to shared care should be explained to the patient and accepted by them. Patients are under regular follow-up and this provides an opportunity to discuss drug therapy. Intrinsic in the shared care agreement is that the prescribing doctor should be appropriately supported by a system of communication and cooperation in the management of patients. The doctor who prescribes the medicine has the clinical responsibility for the drug and the consequence of its use**.**

Consultant

1. Ensure that the patient/carer is an informed recipient in therapy.
2. Ensure that the patient/care understands their treatment regimen and any monitoring or follow up that is required (using advocacy if appropriate). Issue any local patient information leaflets where appropriate.
3. Ensure baseline investigations are normal before commencing treatment.
4. Initiate treatment and prescribe until the GP formally agrees to share care (as a minimum, supply the first 2 months of treatment or until the patient is stabilised).
5. Send a letter to the GP requesting shared care for this patient.
6. Clinical supervision of the patient by routine clinic follow-up on a regular basis.
7. Send a letter/results notification to the GP after each clinic attendance ensuring current dose, and if applicable, most recent blood results and frequency of monitoring are stated.
8. Evaluation of any reported adverse effects by GP or patient.
9. Advise GP on review, duration or discontinuation of treatment where necessary. Where urgent action is required following tests the hospital team will telephone the patient and inform GP.
10. Inform GP of patients who do not attend clinic appointments.
11. Discuss benefits of treatment, risks in pregnancy and breastfeeding with the patient. Counsel the patient on contraception (if appropriate) and what to do if pregnancy occurs. Document in the patient's notes.
12. Ensure that backup advice is available at all times.

General Practitioner

1. Ensure that the patient/carer understands the nature, effect and potential side effects of the drug before prescribing it as part of the shared care programme and contact the specialist for clarification where appropriate.
2. Monitor patient's overall health and well-being.
3. Report any adverse events to the consultant, where appropriate.
4. Report any adverse events to the MHRA / CHM, where appropriate.
5. Help in monitoring the progression of disease.
6. Prescribe the drug treatment as described.
7. Provide contraception advice and prescription as appropriate. Prescribe folic acid if appropriate.

City and Hackney Medicines Management Team

1. To provide feedback to acute trusts via Joint Prescribing and Medicines Management Group.
2. To support GPs to make the decision whether or not to accept clinical responsibility for prescribing.
3. To support acute trusts in resolving issues that may arise as a result of shared care.

Patient/ Carer

1. Report any adverse effects to their GP and/or specialist

2. Ensure they have a clear understanding of their treatment.
3. Report any changes in disease symptoms to GP and/or specialist
4. Alert GP and/or specialist of any changes of circumstance which could affect management of disease e.g. plans for pregnancy.
5. Take/ administer the medication as prescribed.
6. Undertake any monitoring as requested by the GP and/or specialist.

Costs

Drug Product	Cost in primary care
Oxcarbazepine film coated tablets	**150 mg,** 50-tab pack = £9.29; **300 mg,** 50-tab pack = £19.03; **600 mg,** 50-tab pack = £39.68. *Patients may need to be maintained on a specific manufacturer's branded or generic oxcarbazepine product.
Trileptal® sugar free Oxcarbazepine oral suspension	**300 mg/5 mL,** 250 mL (with oral syringe) = £48.96.

Based on BNF edition 73 (March 2017).

RESOURCES AVAILABLE

- Epilepsy Society accessible via https://www.epilepsysociety.org.uk
- Epilepsy Action accessible via https://www.epilepsy.org.uk

Relevant contact details	
Consultant or Registrar on-call via switchboard	020 8510 5555
Clinical Nurse Specialist	020 8510 5912
Homerton University Hospital NHS Foundation Medicines Information	020 8510 7000
City and Hackney Medicines Management Team	0203 816 3224

References

- SCG template adapted from NELMMN and Barts Health NHS Trust
- Joint Formulary Committee. British National Formulary edition 73. Available at https://ebnf.homerton.nhs.uk [accessed 08/06/2017].
- Summary of product characteristics – Trileptal® 150 mg, 300 mg, 600 mg film-coated tablets. Available at www.medicines.org.uk [accessed 08/06/2017].
- Royal College of Obstetricians & Gynaecologists. Epilepsy in pregnancy, green-top guideline 68. Available at https://www.rcog.org.uk/globalassets/documents/guidelines/green-top-guidelines/gtg68_epilepsy.pdf [accessed 21/06/2017].

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