City and Hackney Clinical Commissioning Group
Homerton University Hospital Foundation Trust

**SHARED CARE GUIDELINE**

# PERAMPANEL

**Treatment of epilepsy in adults and adolescents from 12 years**

***DOCUMENT TO BE SCANNED INTO ELECTRONIC RECORDS AND FILED IN NOTES***

## INTRODUCTION – Indication and Licensing

Perampanel is a first-in-class selective, non-competitive antagonist of the ionotropic α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) glutamate receptor on post-synaptic neurons. The precise mechanism by which perampanel exerts its antiepileptic effects in humans is unknown.

**Licensed indications:**

- Adjunctive treatment of partial-onset (focal) seizures with or without secondarily generalised seizures.
- Adjunctive treatment of primary generalised tonic-clonic seizures in those with idiopathic generalised epilepsy.

## 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 | Consultant Epileptologist | 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 | 2mg once daily | Increase according to response and tolerability in 2mg steps at intervals of at least 2 weeks.<br>*Usual maintenance:* 4 – 8mg once daily. | 12mg once daily |
| Mild or moderate hepatic impairment | 2mg once daily | Increase according to response and tolerability in 2mg steps at intervals of at least 2 weeks. | 8mg once daily |
| Renal impairment | *Mild (eGFR 60-89ml/min/1.73m$^2$)* – no dosing adjustment required.<br>*Moderate to severe or on dialysis (eGFR <60ml/min/1.73m$^2$)* – **AVOID** perampanel.<br>* Note the summary of characteristics did not specify the creatinine clearance values therefore the above eGFR ranges have been based on the the Modification of Diet in Renal Disease Study (MDRD) formula. | | |
| Patients ≥65 years | No dosing adjustment required. | | |

**Other considerations:**

- To be taken once daily before bedtime.
- May be taken with or without food.
- The tablet should be swallowed whole with a glass of water. It should not be chewed, crushed or split.
- The tablet cannot be split accurately as there is no break line.
- **Single missed dose** – perampanel has a long half-life, the patient should wait and take their next dose as scheduled.
- **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 5mg 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

- **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 perampanel.
- There appears to be an **increased risk of falls**, particularly in the elderly; the underlying reason is unclear.
- Caution should be exercised in patients with a history of substance abuse and the patient should be monitored for symptoms of perampanel abuse.

## CONTRAINDICATIONS

- Severe hepatic impairment (Child-Pugh C).
- Moderate to severe renal impairment or those on dialysis.
- Patients with rare hereditary problems of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption.

## INTERACTIONS

- **Antiepileptic drugs**
    - Plasma concentration of perampanel **reduced** by carbamazepine, fosphenytoin, phenytoin, topiramate and oxcarbazepine (concentration of oxcarbazepine also increased by perampanel).
    - Plasma concentration of midazolam **reduced** by perampanel.
- **Progestogens** - Perampanel accelerates metabolism of progestogens. At doses of 12 mg/day perampanel may decrease the effectiveness of progestative-containing hormonal contraceptives, in this circumstance, additional non-hormonal forms of contraception are recommended.
- **Alcohol** - the effects of perampanel on tasks involving alertness and vigilance such as driving ability are additive or supra-additive to the effects of alcohol.
- **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

**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 4).

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## 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)* |
|---|---|---|
| Dizziness and somnolence (drowsiness, sleepiness) | When symptoms affect activities or increasing risk of falls. | Advise patient not to drive a vehicle, operate complex machinery or engage in other potentially hazardous activities.<br>**Reduce dose if severe** after discussion with the specialist team. |
| Ataxia and dysarthria | Difficulty in speaking and poor balance | **Reduce dose if severe** after discussion with the specialist team. |
| Aggression, anger and irritability | Thoughts of harming others, physical assault or threatening behaviour | **Discuss with the specialist team first.** Reduce dose if significant changes in mood or patterns of behaviour. Stop drug if symptoms are severe. |
| Perampanel (Fycompa®) is a black triangle drug (▼) therefore all suspected adverse effects will need to be reported to the Medicines and Healthcare products Regulatory Agency (MHRA) via the Yellow Card Scheme. | | |

**Patients should be monitored for signs of suicidal ideation and behaviours and appropriate treatment should be considered. Patients (and caregivers of patients) 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 are limited amounts of data (less than 300 pregnancy outcomes) from the use of perampanel in pregnant women. 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).
- **Breastfeeding** – it is not known whether perampanel is excreted in human milk. Studies in lactating rats have shown excretion of perampanel and/or its metabolites in milk. The specialist team will discuss this with the patient.
- **Fertility** – the effect of perampanel on human fertility has not been established. Studies in rats have not shown any effects on early embryonic development and on male fertility.

**For comprehensive information please refer to the <u>current</u> British National Formulary and Summary of Product Characteristics.**

## SHARED CARE

**<u>Shared care guideline</u>*:*** 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 <u>out responsibilities for each party</u>. 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 patient/carer 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 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 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 |
|---|---|
| Fycompa® film coated perampanel tablets | **2 mg** (orange) 7-tab pack = £35.00; **4 mg** (red) 28-tab pack = £140.00; **6 mg** (pink) 28-tab pack = £140.00; **8 mg** (purple) 28-tab pack = £140.00; **10 mg** (green) 28-tab pack = £140.00; **12 mg** (blue) 28-tab pack = £140.00. |

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 01/06/2017].
- Summary of product characteristics – Fycompa® 2mg, 4mg, 6mg, 8mg, 10mg, 12mg film-coated tablets. Available at www.medicines.org.uk [accessed 01/06/2017].
- 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]


Date SCG approved by Joint Prescribing Group (JPG): 11/2017 Review date: 11/2020