Perampanel *(Fycompa®)* (Amber with Shared Care)

Shared Care Guidelines: For the adjunctive therapy in the treatment of partial-onset seizures, with or without secondary generalisation, in patients with epilepsy aged 12 years and older.

AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of Perampanel for epileptic seizures 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.

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 the 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 antiepileptic 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 (every 2-5 years).
4	Discuss the benefits, side-effects and possible drug interactions of Perampanel 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 perampanel.
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 perampanel, 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 perampanel 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.
16	Supply GP with summary within 14 days of a hospital out-patient review or in-patient stay.

	General Practitioner responsibilities
1	Reply to the request for shared care as soon as practicable.
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 perampanel after the initial 1 month of treatment under specialist care, provided the patient has been stabilised on a maintenance dose by then.
4	Prescribe perampanel at the dose recommended.
5	Ensure compatibility of perampanel with other concomitant medication.
6	Monitor the patient's response to treatment; make dose adjustments as agreed with specialist.
7	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.

8	Refer promptly to specialist when any loss of clinical efficacy is suspected (e.g. worsening of disease-related symptoms, new symptoms suggestive of disease recurrence or progression) or intolerance to therapy occurs.
9	Stop treatment, or initiate its tapered withdrawal, on the advice of the specialist.

Patient's role	
1	Report to the specialist or GP if he or she does not have a clear understanding of the treatment.
2	Share any concerns in relation to treatment with medicine.
3	Report any adverse effects to the specialist or GP whilst taking the medicine.

BACK-UP ADVICE AND SUPPORT

Contact details	Telephone No.	Email address:
Sarah Davis (Epilepsy Nurse)	01225 825856	Sarah.davis22@nhs.net
Hospital Pharmacy Dept:	01225 824640	
Dr Nicola Giffin (Consultant Neurologist)	01225 825456	Nicola.giffin@nhs.net

Points for the GP to pass onto the patient:

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 perampanel 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 perampanel.

Patient information leaflet can be found here: https://www.medicines.org.uk/emc/product/7876/pil

SUPPORTING INFORMATION

Summary of condition and licensed indications.

Perampanel is a new antiepileptic drug (AED) with a novel mode of action that is licensed for add-on therapy of refractory partial epilepsy. Perampanel is a once-daily tablet, which may help facilitate good compliance

Background

It is estimated that about 20-30% of patients with partial epilepsy do not achieve reasonable sustained remission with optimal anti-epileptic medication and/or suffer from significant adverse effects. Recently introduced anti-epileptic drugs have been developed in order to improve the benefit risk/balance of the standard therapy. Usually, 20 to 40% of patients obtained a 50% or greater reduction in the frequency of seizures with novel anti-epileptic drug, as compared to baseline. Perampanel is a new adjunctive therapeutic option for these patients.
Perampanel must be initiated by epilepsy specialists.

The medicine is indicated for:

- adjunctive therapy in the treatment of partial-onset seizures, with or without secondary generalisation, in patients with epilepsy aged 12 years and older.

Treatment Aims (Therapeutic plan)

Perampanel will be used for patients with partial epilepsy who do not achieve reasonable sustained remission with optimal anti-epileptic medication and/or suffer from significant adverse effects.

Treatment Schedule (including dosage and administration)

Treatment with perampanel should be initiated at a dose of 2 mg once a day. The dose may be increased based on clinical response and tolerability, by increments of 2 mg (at intervals of 1- 2 weeks, see further details below) to a maintenance dose of between 4 mg once day and 8 mg once a day. The dose may be further increased by increments of 2 mg to a maximum dose of 12 mg once a day, depending upon individual clinical response and tolerability at a dose of 8 mg once day. Doses should be titrated at intervals of at least 1 week for patients who are taking concomitant medicinal products that shorten the half-life of perampanel (e.g. Oxcarbazepine Carbamazepine, Phenytoin) and at intervals of a minimum of 2 weeks for all other patients. Perampanel should be taken as single oral dose at bedtime. It may be taken with or without food. The tablet should be swallowed whole with a glass of water at

bedtime. It should not be chewed, crushed or split. The tablets cannot be split accurately as there is no break line. To ensure the patient receives the entire dose the tablets should be swallowed whole without chewing or crushing.

Missed doses

Single missed dose: As perampanel has a long half-life, the patient should wait and take their next dose as scheduled.

If more than 1 dose has been missed, for a continuous period of less than 5 half-lives (3 weeks for patients not taking perampanel metabolism-inducing anti-epileptic drugs (AED), 1 week for patients taking perampanel metabolism-inducing AEDs), consideration should be given to re-start treatment from the last dose level.

If a patient has discontinued perampanel for a continuous period of more than 5 half-lives, it is recommended that initial dosing recommendations given above should be followed.

Contra-indications and precautions for use

Hypersensitivity to the active substance or to any of the excipients

Cautions

Perampanel may cause dizziness and somnolence and therefore may influence the ability to drive or use machines. Do not exceed a maximum daily dose of 8mg in mild to moderate hepatic impairment. Avoid perampanel in severe hepatic impairment. Avoid perampanel in moderate to severe renal impairment. Perampanel is not recommended in women of childbearing potential not using contraception unless clearly necessary.

Pregnancy

There are limited amounts of data (less than 300 pregnancy outcomes) from the use of perampanel in pregnant women. Studies in animals did not indicate any teratogenic effects in rats or rabbits, but embryotoxicity was observed in rats at maternally toxic doses. Perampanel is not recommended during pregnancy.

Breastfeeding Studies in lactating rats have shown excretion of perampanel and / or its metabolites in milk. It is not known whether perampanel is excreted in human milk. A risk to the newborns / infants cannot be excluded. A decision must be made whether to discontinue breastfeeding or to discontinue / abstain from perampanel therapy taking into account the benefit of breastfeeding for the child and the benefit of therapy for the woman.

Side-effects

Perampanel was launched in July 2012 and no longer has black triangle status (▼).

Very common (≥10%): dizziness and somnolence. The nature and frequency of the adverse events is dose related, occurs mainly in the titration period and seems comparable to those of other antiepileptic drugs. The prevalence of adverse effects decreases with treatment duration. Paediatric population: Based on the clinical trial database, the frequency, type and severity of adverse reactions in adolescents are expected to be the same as in adults. Refer to the SPC for a full list of adverse effects.

Adverse-effects of note:

- Perampanel can cause signs of dizziness, diplopia, unsteadiness (falls in elderly patients) or behavioural changes. If these symptoms are troublesome, discuss with a specialist as soon as possible.
- Use in moderate or severe renal impairment and severe hepatic impairment is not recommended.
- Suicidal ideation has been identified in a small number of people being treated with anti-epileptics. Therefore patients (and caregivers of patients) should be advised to seek medical advice should signs of suicidal ideation or behaviour emerge.
- Aggression and hostile behaviour has been reported in patients receiving perampanel therapy (more frequently at higher doses). Most of the reported events were either mild or moderate and patients recovered either spontaneously or with dose adjustment. The dosage of perampanel should be reduced if such symptoms occur and should be discontinued immediately if symptoms are severe.
- Abuse potential - caution should be exercised in patients with a history of substance abuse and the patient should be monitored for symptoms of perampanel abuse.

Serious suspected reactions (even if well recognised or causal link uncertain) should be reported to the MHRA.

Monitoring

At the time of approval no specific monitoring was required for perampanel other than seizure control.

Drug Interactions

Perampanel is not considered a strong inducer or inhibitor of cytochrome P450 or UGT enzymes.

Oral Contraceptives

In healthy women receiving 12 mg (but not 4 or 8 mg/day) for 21 days concomitantly with a combined oral contraceptive, perampanel was shown to decrease the levonorgestrel exposure (mean Cmax and AUC values were each decreased by 40%). Ethinylestradiol AUC was not affected by perampanel 12 mg whereas Cmax was decreased by 18%. Therefore, the possibility of decreased efficacy of progesterone - containing oral contraceptives should be considered for women needing perampanel 12 mg/day and in these patients an additional reliable method (intrauterine device (IUD), condom) should be used.

Anti-epileptic drugs
Some anti-epileptic drugs known as enzyme inducers (carbamazepine, phenytoin, oxcarbazepine) have been shown to increase perampanel clearance and consequently to decrease plasma concentrations of perampanel. In a population pharmacokinetic analysis of patients with partial- onset seizures receiving perampanel up to 12 mg/day in placebo-controlled clinical trials, the total clearance of perampanel was increased when administered with carbamazepine (3-fold), phenytoin (2-fold) and oxcarbazepine (2-fold), which are known inducers of enzymes of metabolism. This effect should be taken into account and managed when adding or withdrawing these anti-epileptic drugs from a patient's treatment regimen.

Also see BNF appendix 1 and SPC.

Cost
At current prices (July 2018), one year's treatment with medicine at the maintenance dose is £1825

References

Summary of Product Characteristics Perampanel (Fycompa®) Electronic Medicines Compendium https://www.medicines.org.uk/emc/product/7876/smpc

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Document details
July 2018, Sarah Davis, Epilepsy Clinical Nurse Specialist, RUH and Dr Rachel Hobson, Formulary Pharmacist, NHS Wiltshire CCG on behalf of BaNES CCG.