North Central London
Joint Formulary Committee

Factsheet

PERAMPANEL (Fycompa®)

As Adjunct Treatment In Partial Seizures With Or Without Secondary Generalisation

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FACTSHEET TO FACILITATE PRESCRIBING

PLEASE NOTE THIS IS NOT A SHARED CARE GUIDELINE, NOR IS IT A FULL SUMMARY OF DRUG INFORMATION. ALWAYS REFER TO THE MOST RECENT BNF AND/OR SUMMARY OF PRODUCT CHARACTERISTICS.

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Factsheet –PERAMPANEL (Fycompa®) for adjunct treatment in partial seizure with or without secondary generalisation

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

As per local formulary agreement, perampanel is restricted to consultant neurologist and is for refractory patients who have failed or not tolerated other options.

The hospital team will:

1. Provide the patient with initial information regarding the treatment and possible adverse effects.
2. Initiate and optimise (stabilise) treatment and inform GP when patient is stable on dose so that GP can continue prescribing (timescale will be dependent on individual dose titration but typically after 3 months).
3. Change dose if necessary and inform patient and GP of dose changes.
4. Clinically supervise patient by routine clinic follow-ups every 4-6 months and monitor response to treatment.

Dose and Administration

The maximum licensed dose is 12 mg/day; however perampanel at doses of 4mg/day to 12mg/day has shown to be effective therapy in partial-onset seizures.

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. The tablets cannot be split accurately as there is no break line.

Renal impairment*:* dose adjustment is not required in patients with mild renal impairment. Use in patients with moderate or severe renal impairment or patients undergoing haemodialysis is not recommended.

Hepatic impairment*:* dosing for patients with mild and moderate impairment should not exceed 8 mg. Use in patients with severe hepatic impairment is not recommended.

Discontinuing treatment: It is recommended that discontinuation be undertaken gradually to minimise the potential for rebound seizures. However, due to its long half-life and subsequent slow decline in plasma concentrations, perampanel can be discontinued abruptly if absolutely needed. GPs may need to stop treatment on advice of specialist or immediately if urgent need arises. If unsure about urgency of discontinuation please contact specialist.

Adverse Effects

Very common (≥10%): Dizziness and somnolence. The nature and frequency of the adverse events was dose related, occurred mainly in the titration period and seemed comparable to those of other antiepileptic drugs. The prevalence of adverse effects decreased with treatment duration.

Reporting all *serious* suspected adverse reactions for established medicinal products is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report suspected serious adverse reactions for this medicine using the Yellow Card Scheme.

Contraindications

Hypersensitivity to the active substance or to any of the excipients.

Special Warnings and Precautions for Use

Suicidal ideation: Suicidal ideation and behaviour have been reported in patients treated with anti-epileptic medicinal products in several indications. A meta-analysis of randomised placebo controlled trials of antiepileptic medicinal products has also shown a small increased risk of suicidal ideation and behaviour. The mechanism of this risk is not known and the available data do not exclude the possibility of an increased risk for perampanel.
Therefore, 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.

Severe cutaneous adverse reactions (SCARs) including drug reaction with eosinophilia and systemic symptoms (DRESS):

Severe cutaneous adverse reactions (SCARs) including drug reaction with eosinophilia and systemic symptoms (DRESS), which can be life-threatening or fatal, have been reported in association with perampanel treatment.

At the time of prescription patients should be advised of the signs and symptoms and monitored closely for skin reactions. Symptoms of DRESS include typically, although not exclusively, fever, rash associated with other organ system involvement, lymphadenopathy, liver function tests abnormalities and eosinophilia. It is important to note that early manifestations of hypersensitivity, such as fever or lymphadenopathy, may be present even though rash is not evident. If signs and symptoms suggestive of these reactions appear, perampanel should be withdrawn immediately and an alternative treatment considered (as appropriate).

Effects on ability to drive and operate machinery: Perampanel may cause dizziness and somnolence and therefore may influence the ability to drive or use machines. Patients are advised not to drive a vehicle, operate complex machinery or engage in other potentially hazardous activities until it is known whether perampanel affects their ability to perform these tasks.
Please contact the hospital team in the first instance if side effects prove to be troublesome to the patient as it may be necessary to reduce the dose.

Falls: There appears to be an increased risk of falls, particularly in the elderly; the underlying reason is unclear.

Aggression: Aggressive and hostile behaviour has been reported in patients receiving perampanel therapy. In perampanel-treated patients in clinical trials, aggression, anger and irritability were reported more frequently at higher doses. Most of the reported events were either mild or moderate and patients recovered either spontaneously or with dose adjustment. However, thoughts of harming others, physical assault or threatening behaviour were observed in some patients (< 1% in perampanel clinical studies). Patients and caregivers should be counselled to alert a healthcare professional immediately if significant changes in mood or patterns of behaviour are noted. 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.

Other concomitant (non- anti-epileptic) cytochrome P450 inducing or inhibiting medicinal products: Patients should be closely monitored for tolerability and clinical response when adding or removing cytochrome P450 inducers or inhibitors, since perampanel plasma levels can be decreased or increased; the dose of perampanel may need to be adjusted accordingly.

Perampanel contains lactose, therefore patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Pregnancy and Breastfeeding: Perampanel is not recommended during pregnancy. Perampanel is not recommended in women of childbearing potential not using contraception unless clearly necessary. 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.

Perampanel is classified as a Category 2 medicine for generic prescribing:

https://www.gov.uk/drug-safety-update/antiepileptic-drugs-updated-advice-on-switching-between-different-manufacturers-products

Base the need for continued supply of a particular manufacturer's product on clinical judgement and consultation with patient and/or carer, taking into account factors such as seizure frequency and treatment history. Take into account patient/carer-related factors such as their negative perceptions about alternative products and/or other issues related to the patient should also be taken into account.

Drug Interactions

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

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. Ethinylestradiol was not affected by perampanel 12 mg. Therefore, the possibility of decreased efficacy of **progesterone-containing oral contraceptives** should be considered for women needing perampanel 12 mg/day and an additional reliable method of contraception (intra-uterine device (IUD), condom) should be used.

Some **anti-epileptic drugs** known as **CYP450 3A enzyme inducers** (carbamazepine, phenytoin, oxcarbazepine) have been shown to increase perampanel clearance and consequently to decrease plasma concentrations of perampanel. Conversely, withdrawal of a concomitant CYP450 3A enzyme inducer can be expected to increase plasma concentrations of perampanel and dose reduction may be required. In a population pharmacokinetic analysis of patients receiving perampanel up to 12 mg/day, the total clearance of perampanel was increased when administered with carbamazepine (3-fold), phenytoin (2-fold) and oxcarbazepine (2-fold). This effect should be taken into account and managed when adding or withdrawing these anti-epileptic drugs from a patient's treatment regimen.

Please refer to SPC/BNF for full information on interactions between perampanel and other anti-epileptic drugs and how to manage these interactions.

Clinical Monitoring

At the time of approval no specific monitoring was required for perampanel other than seizure control. GP's should review their patients as per their normal practice.

Contact Details

University College London Hospital NHS Foundation Trust

Department of Clinical and Experimental Epilepsy

Please see individual consultant secretaries below

Professor Duncan/Dr Heaney/Mrs Susan Usiskin	Gaby.baykarali@uclh.nhs.uk
Professor Walker/Professor Sander/ Dr S O'Sullivan/Dr Meneka Sidhu	Amanda.orie@uclh.nhs.uk
Dr Eriksson	Maggie.moore@uclh.nhs.uk
Dr Rugg-Gunn/Dr Sanjeev /Dr Rajakulendran/Epilepsy nurses	Kimberly.Burden@uclh.nhs.uk
Dr Diehl/ Professor Koepp/Dr Chowdhury	Mary.Fanning@uclh.nhs.uk

Epilepsy Nurse Specialists – Tel: 0203 448 8627; epilepsy@uclh.nhs.uk

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- Summary of Product Characteristics for Fycompa, Eisai Europe Ltd can be accessed via http://www.medicines.org.uk/emc/medicine/26951/SPC/Fycompa
- BNF - http://www.bnf.org/bnf/index.htm