Specialist Initiated Drugs

Prescribing Information Sheet September 2014

Lacosamide (Vimpat®) - Adjunctive treatment of partial-onset seizures

Formulary Status

Lacosamide for the adjunctive treatment of partial-onset seizures should be initiated by a specialist who will prescribe the initial supply.

The specialist will titrate the dose until the patient is stable. This usually takes 1 -2 months but will vary per patient.

On-going prescribing can be continued by a GP.

The responsibility for increasing/decreasing the dose or stopping treatment due to lack of effect or side effects remains with the specialist. They should be consulted if a change in treatment is required.

Full prescribing guidance – Summary of Product Characteristics
www.emc.medicines.org.uk

Indication and Dosage

Indication- Lacosamide is indicated for the adjunctive treatment of partial-onset seizures with or without secondary generalisation in adult and adolescent (16-18 years) patients with epilepsy.

Presentation- Film coated tablets 50mg, 100mg, 150mg, 200mg. Costs are equivalent per mg for tablet strengths 50mg, 100mg and 150mg. The 200mg strength is cheaper than combinations of other strengths. Syrup 10mg/ml

Dosage and Administration – Lacosamide is taken as a twice daily dose with or without food.

The recommended starting dose is lacosamide 50mg twice daily which should be increased to an initial therapeutic dose of 100mg twice daily after one week. Depending on response and tolerability, the maintenance dose can be further increased by 50mg twice a day each week to a maximum recommended daily dose of 400mg (200mg twice daily)

Renal impairment - No dose adjustment is necessary in mildly and moderately renally impaired patients (CL_{CR} >30 ml/min). In patients with mild or moderate renal impairment, a loading dose of 200 mg may be considered, but further dose titration (>200 mg daily) should be performed with caution. In patients with severe renal impairment (CL_{CR} ≤30 ml/min) and in patients with endstage renal disease, a maximum maintenance dose of 250 mg/day is recommended. In these patients, the dose titration should be performed with caution.

Approved by: East Kent Prescribing Group *(Representing Ashford CCG, Canterbury and Coastal CCG, South Kent Coast CCG and Thanet CCG)*
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Hepatic impairment – No dose adjustment is required for patients with mild to moderate hepatic impairment. Titrate with caution in mild to moderate impairment if co-existing renal impairment; caution in severe impairment—no information available

Monitoring
No specific monitoring requirements are highlighted in the SPC

End of treatment
It is recommended that discontinuation be undertaken gradually to minimise the potential for rebound seizures (The manufacturers advise tapering the daily dose, for example, by 200 mg/week but seek advice of the Specialist).

Special warnings, precautions for use and adverse effects (consult SPC for full list)

Contraindications
Known second- or third-degree atrioventricular (AV) block.

Cautions
Use with caution in patients with known conduction problems, severe cardiac disease or in elderly. Prolongation of the PR interval with lacosamide has been observed. Use with caution in patients treated with products associated with PR prolongation e.g. venlafaxine, pregabalin, carbamazepine, lamotrigine and those treated with class I antiarrhythmic drugs e.g. flecainide, disopyramide

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 lacosamide

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.

Nervous system and gastrointestinal disorders
The most frequently reported adverse reactions in trials with lacosamide were dizziness, headache, nausea and diplopia which were usually mild to moderate in intensity. Some were dose-related and were alleviated by reducing the dose. The incidence and severity of central nervous system and gastrointestinal adverse reactions usually decreased over time.

Falls
Treatment with lacosamide has been associated with dizziness which could potentially increase the occurrence of accidental injury or falls. Therefore, patients should be advised to be cautious until they are familiar with the potential effects of lacosamide.

Drug Interactions (consult SPC for full list)

Interactions listed in BNF 67 (March 2014) are with medications that antagonise the effects of anti-epileptics such as antidepressants, antimalarials, antipsychotics and orlistat.

Drugs associated with PR prolongation
Lacosamide should be used with caution in patients treated with drugs associated with PR prolongation (e.g., carbamazepine, lamotrigine, pregabalin), class I antiarrhythmics, rifampicin, St John's Wort, phenytoin, phenobarbital, fluconazole, itraconazole, ketoconazole, ritonavir, clarithromycin. However, subgroup analysis did not identify an increased magnitude of PR prolongation in patients with concomitant administration of carbamazepine or lamotrigine in clinical trials

Concomitant anti-epileptic drugs
In interaction trials lacosamide did not significantly affect the plasma concentrations of carbamazepine and valproic acid. Lacosamide plasma concentrations were not affected by carbamazepine and by valproic acid. A population PK analysis estimated that concomitant treatment with other anti-epileptic drugs known to be enzyme inducers (carbamazepine, phenytoin, phenobarbital, in various doses) decreased the overall systemic exposure of lacosamide by 25%.

Enzyme inducing drugs
Strong enzyme inducers such as rifampicin or St John's Wort may moderately reduce the levels of lacosamide
Caution is recommended in concomitant treatment with strong inhibitors of CYP2C9 (e.g. fluconazole) and CYP3A4 (e.g. itraconazole, ketoconazole, ritonavir, clarithromycin), which may lead to increased systemic exposure of lacosamide. Such interactions have not been established *in vivo* but are possible based on *in vitro* data.

Oral contraceptives
In an interaction trial there was no clinically relevant interaction between lacosamide and the oral contraceptives ethinylestradiol and levonorgestrel. Progesterone concentrations were not affected when the medicinal products were co-administered.

Contact details of Specialist Team

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References

Summary of Product Characteristics- Vimpat® 50mg, 100mg, 150mg &200mg tablets, 10mg/ml syrup and 10mg/ml solution for infusion .UCB Pharma Ltd. Last updated 13 May 2014 www.emc.medicines.org.uk

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NICE CG137 The epilepsies: the diagnosis and management of the epilepsies in adults and children in primary and secondary care January 2012 www.nice.org.uk