

LACOSAMIDE

as adjunct treatment in partial epilepsy with or without secondary generalisation in patients over the age of 16

SHARED CARE CRITERIA

Dear GP

This shared care arrangement outlines suggested ways in which the responsibilities for managing the prescribing of lacosamide for patients over the age of 16 with partial-onset seizures with or without secondary generalisation can be shared between the specialist and yourselves as the patient's general practitioner and the patient.

Initial dose titration will take place under the care of the Consultant Neurologist at the National Hospital for Neurology and Neurosurgery. Once the patient has been established on a dose of lacosamide and has been stable for 3 months the GP will continue care under the supervision of the Consultant Neurologist.

RESPONSIBILITIES

Consultant Neurologist

1. Provide the patient with initial information regarding the treatment and possible adverse effects.
2. Provide a seizure diary.
3. Baseline ECG monitoring in all patients and follow up ECG in high risk patients.
4. Initiate and optimise (stabilise) treatment, and continue to prescribe until the GP formally agrees to shared care.
5. Send a letter to the GP suggesting that shared care is agreed for this patient.
6. Inform patient of shared care arrangements.
7. Clinically supervise patient by routine clinic follow-ups.
8. Change dose if necessary and inform patient and GP of dose changes.
9. Evaluate adverse effects reported by GP or patient.
10. Communicate the results of tests performed in secondary care to GP.
11. Provide a review date and identify who is to perform this.
12. Ensure that backup advice is accessible at all times.
13. Proactively monitor patient for adverse effects of lacosamide including suicidal ideation and behaviour, cardiac rhythm and conduction abnormalities.

General Practitioner

1. Monitor patient's overall health and wellbeing.
2. Monitor adverse effects and possible medicines interactions.
3. Report any adverse effects reported by the patient to the Epilepsy team.
4. Prescribe maintenance lacosamide therapy and adjust dose on recommendation of consultant.
5. Inform patient of changes in dose.

Patient/Carer

1. Monitor seizure activity in seizure diary.
2. Report any adverse effects to the Consultant Neurologist or GP.
3. Share any concerns in relation to the treatment with lacosamide.
4. Report to the Consultant Neurologist or GP if they do not have clear understanding of their treatment.

Clinical Commissioning Group

1. To support GPs to decide whether or not to accept clinical responsibility for prescribing.
2. To support Trusts in resolving issues that may arise as a result of shared care.

LACOSAMIDE

as adjunct treatment in partial epilepsy with or without secondary generalisation in patients over the age of 16

LICENSED INDICATION (relevant to this Shared Care Guideline)

Lacosamide is indicated as adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in patients with epilepsy aged 16 years and older.

DOSE AND ADMINISTRATION

Lacosamide must be taken twice a day. The recommended starting dose is 50 mg twice a day which should be increased to an initial therapeutic dose of 100 mg twice a day after one week.

Depending on response and tolerability, the maintenance dose can be further increased by 50 mg twice a day every week, to a maximum recommended daily dose of 400 mg (200 mg twice a day). Lacosamide may be taken with or without food. In accordance with the current clinical practice, if lacosamide has to be discontinued, it is recommended that this be done gradually as per specialist advice.

Dosing in renal impairment:

No dose adjustment is necessary in mildly and moderately renally impaired patients ($CL_{CR} > 30$ ml/min). In patients with severe renal impairment ($CL_{CR} \leq 30$ ml/min) and in patients with end stage renal disease, a maximum maintenance dose of 250 mg/day is recommended. In these patients, the dose titration should be performed with caution as there is little clinical experience.

Dosing in hepatic impairment

No dose adjustment is needed for patients with mild to moderate hepatic impairment. The dose titration in these patients should be performed with caution considering co-existing renal impairment.

Titration to doses > 200mg daily should also be performed with caution.

The pharmacokinetics of lacosamide has not been evaluated in severely hepatic impaired patients.

Dosing in elderly (over 65 years of age)

No dose reduction is necessary in elderly patients. The experience with lacosamide in elderly patients with epilepsy is limited. Age associated decreased renal clearance with an increase in AUC levels should be considered in elderly patients.

ADVERSE EFFECTS

Very common ($\geq 10\%$) adverse effects include dizziness, headache, diplopia and nausea.

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.

Description of selected adverse reactions

The use of lacosamide is associated with dose-related increase in the PR interval. Adverse reactions associated with PR interval prolongation (e.g. atrioventricular (AV) block, syncope, bradycardia) may occur.

In clinical trials in epilepsy patients the incidence rate of reported first degree AV block was uncommon (0.7%, 0%, 0.5% and 0% for lacosamide 200 mg, 400 mg, 600 mg or placebo respectively). Cases with second and third degree AV block associated with lacosamide treatment have been reported in post-marketing experience.

In clinical trials the incidence rate for syncope was uncommon and did not differ between lacosamide treated epilepsy patients (0.1%) and placebo treated epilepsy patients (0.3%).

Long term lacosamide treatment was not associated with any change of median or mean haematology, clinical chemistry, vital signs or body weight. ECG showed a small increase in the median PR interval (5-9ms across all subjects)

For a more detailed profile please refer to the [Summary Product Characteristics of lacosamide](#).

CAUTIONS AND CONTRAINDICATIONS

Contraindications:

Tablets and syrup:

- Hypersensitivity to the active substance or to any of the excipients.
- Known second- or third-degree atrioventricular (AV) block.

The information contained in this guideline is issued on the understanding that it is accurate based on the resources at the time of issue. For further information please refer to the most recent Summary of Product Characteristics and British National Formulary.

LACOSAMIDE

as adjunct treatment in partial epilepsy with or without secondary generalisation in patients over the age of 16

Cautions:

Dizziness

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

Cardiac Rhythm and Conduction

Prolongations in PR interval with lacosamide have been observed in clinical studies. Lacosamide should be used with caution in patients with known conduction problems or severe cardiac disease such as a history of myocardial infarction or heart failure. Caution should especially be exerted when treating elderly patients as they may be at an increased risk of cardiac disorders or when lacosamide is used in combination with products known to be associated with PR prolongation.

Second degree or higher AV block has been reported in post-marketing experience. In the placebo-controlled trials of lacosamide in epilepsy patients, atrial fibrillation or flutters were not reported; however both have been reported in open-label epilepsy trials and in post-marketing experience. Patients should be made aware of the symptoms of second-degree or higher AV block (e.g. slow or irregular pulse, feeling lightheaded and fainting) and of the symptoms of atrial fibrillation and flutter (e.g. palpitations, rapid or irregular pulse, shortness of breath). Patients should be counseled to seek medical advice should any of these symptoms occur.

Suicidal ideation and behaviour

Suicidal ideation and behaviour have been reported in patients treated with anti-epileptic agents in several indications. A meta-analysis of randomised placebo controlled trials of anti-epileptic drugs 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.

Caution with syrup

Patients with rare hereditary problems of fructose intolerance should not take this medicine. The syrup contains aspartame, a source of phenylalanine, which may be harmful for people with phenylketonuria.

Pregnancy and Lactation

There is no adequate data from the use of lacosamide in pregnant women. Studies in animals did not indicate any teratogenic effects in rats or rabbits, but embryotoxicity was observed in rats and rabbits at maternal toxic doses. The potential risk for humans is unknown. Lacosamide should not be used during pregnancy unless clearly necessary (if the benefit to the mother clearly outweighs the potential risk to the foetus). If women decide to become pregnant, the use of this product should be carefully re-evaluated by a consultant neurologist

It is unknown whether lacosamide is excreted in human breast milk. Animal studies have shown excretion of lacosamide in breast milk. For precautionary measures breast-feeding should be discontinued during treatment with lacosamide.

DRUG INTERACTIONS

Lacosamide should be used with caution in patients treated with medicinal products known to be associated with PR prolongation (e.g. carbamazepine, lamotrigine, pregabalin) and in patients treated with class I antiarrhythmic drugs. However, subgroup analysis did not identify an increased magnitude of PR prolongation in patients with concomitant administration of carbamazepine or lamotrigine in clinical trials.

Strong enzyme inducers such as rifampicin or St John's Wort (*Hypericum perforatum*) may moderately reduce the systemic exposure of lacosamide. Therefore, starting or ending treatment with these enzyme inducers should be done with caution.

In interaction trials lacosamide did not significantly affect the plasma concentrations of carbamazepine and valproic acid. 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

LACOSAMIDE

as adjunct treatment in partial epilepsy with or without secondary generalisation in patients over the age of 16

No data on the interaction of lacosamide with alcohol are available.

Lacosamide has a low protein binding of less than 15%. Therefore, clinically relevant interactions with other drugs through competition for protein binding sites are considered unlikely.

For more details please refer to the [Summary Product Characteristics of lacosamide](#).

CLINICAL MONITORING

Patients should be monitored for seizure control and adverse effects of lacosamide, including signs of suicidal ideation and behaviors.

COST

50 mg x 14 tabs: £10.81	100 mg x 14 tabs: £21.62	150 mg x 14 tabs: £32.44
100 mg x 56 tabs: £86.50	150 mg x 56 tabs: £129.74	200 mg x 56 tabs: £144.16
Syrup (10 mg/ml) x 200 ml: £25.74		

(Drug Tariff November 2014 and BNF 68 September 2014)

CONTACT DETAILS

National Hospital for Neurology & Neurosurgery - Queen Square - London - WC1N 3BG; Switchboard Tel: 020 3456 7890
Department of Clinical and Experimental Epilepsy - Epilepsy specialist nurses Tel: 020 3448 8627; 020 3448 8632 or 020 3448 8863

REFERENCES

- Ben-Menachem E et al. Efficacy and safety of oral lacosamide as adjunctive therapy in adults with partial-onset seizures. *Epilepsia* 2007;48(7):1308-1317
- Halasz P et al. Lacosamide: Efficacy and safety as oral adjunctive therapy in adults with partial seizures. Presented at the EFNS, August 2007, Brussels.
- Chung SS et al. Lacosamide: Efficacy and safety of oral adjunctive treatment for partial onset seizures. Presented at the 61st Annual American Epilepsy Meeting. November 2007. Philadelphia
- Rosenfeld W et al. Lacosamide: An interim evaluation of long-term safety and efficacy as oral adjunctive therapy in subjects with partial-onset seizures. Presented at the 61st Annual American Epilepsy Meeting. November 2007. Philadelphia
- Errinton AC et al. Seeking a mechanism of action for the novel anticonvulsant lacosamide. *Neuropharmacology* 2006; 50:1016-1029
- Beyreuther BK et al: Lacosamide: A review of preclinical properties. *CNS drug reviews* 2007;13:21-42.
- Summary of Product Characteristics for Vimpat® UCB Pharma Limited last updated on eMC on the 15-Aug-2014 accessed via <http://www.medicines.org.uk/emc/medicine/21158> on 12/11/14.

This document represents only a brief summary and is as accurate as possible. Always refer to the Epilepsy team at the National Hospital for Neurology and Neurosurgery for further information.

SCG prepared by Evelyn Frank, Pharmacist UCLH/NHNN November 2008- reviewed June 2012. Approved at NHS NCL Camden Medicines Management Committee July 2009 & June 2012

Reviewed and updated by Kaajal Shah, Pharmacist, UCLH/ NHNN: October 2014

Update agreed at Camden Medicines Management Committee (CMMC): 26 November 2014

Ratified by NCL Medicines Optimisation Group: 02 December 2014

Next Review date October 2017