North Central London
Joint Formulary Committee

Factsheet

Lacosamide (Vimpat®)

Treatment of partial-onset seizures with or without secondary generalisation in patients aged 16 years and older

Start date: February 2020
Review date: February 2023

Document Control		
Date	**Version**	**Action**
February 2020	V1	Factsheet produced by NHNN Agreed by *NCL Shared Care Group*: 04/02/2020

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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NCL JFC is funded by and provides advice to Acute Trusts and Clinical Commissioning Groups in NCL.

Indication information

As per local formulary agreement, Lacosamide is initiated by a Consultant Neurologist and continued by the patients GP for partial-onset seizures with or without secondary generalisation.

The hospital team will:

1. Decide with the patient how they will document their seizure type and frequency. This may be by providing a seizure diary to the patient or agreeing for the patient to document this information in their own diary or electronic device.
2. Perform a baseline ECG in all patients and follow up ECG in high risk patients.
3. Provide the patient with initial information regarding the treatment and possible adverse effects.
    a. In particular, advise patients of the symptoms of cardiac arrhythmia (e.g. slow, rapid or irregular pulse, palpitations, shortness of breath, feeling lightheaded, fainting) & advise to seek immediate medical advice if these symptoms occur.
4. Initiate and optimise (stabilise) treatment and inform GP when patient is stable on dose so that GP can continue prescribing, including whether lacosamide is used as monotherapy or adjuvant therapy (timescale will be dependent on individual dose titration but typically after 3 months).
5. Change dose if necessary and inform patient and GP of dose changes.
6. Clinically supervise patient by routine clinic follow-up and monitor response to treatment. This includes monitoring the patient for adverse effects of lacosamide including suicidal ideation and behaviour, cardiac rhythm and conduction abnormalities

Checklist for GPs:

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

Dose and Administration in adult patients

The maximum licensed dose is 600mg daily as monotherapy or 400mg daily as adjunctive therapy.

Lacosamide must be taken **twice a day** and may be taken with or without food. The initiation of lacosamide is by the Epilepsy Specialist; usual dosing recommendations are shown in Table 1 below.

Table 1 Summary table of dosing recommendations (adolescents and children ≥50kg and adults):

	Monotherapy	**Adjunctive therapy**
Starting dose	50mg to 100mg twice daily	50mg twice daily
Single loading dose (if applicable)	200 mg	200 mg
Titration (incremental steps)	50 mg twice a day (100 mg/day) at weekly intervals	50 mg twice a day (100 mg/day) at weekly intervals
Maximum recommended dose	Up to 300mg twice daily (i.e. up to 600 mg/day)	Up to 200mg twice daily (i.e. up to 400 mg/day)

Monotherapy – additional information

Lacosamide can also be initiated at the dose of 100 mg twice a day based on the physician's assessment of required seizure reduction versus potential side effects.

Consultant Neurologists may sometimes take the view to initiate and titrate more cautiously, at a dose of 50mg once daily and increase by 50mg daily every 1-2 weeks. This again is based on a benefit versus risk assessment. The details of the initiation and titration regime will be communicated to the GP in all patients.

Adjunctive therapy – additional information

Consultant Neurologists may sometimes take the view to initiate and titrate more cautiously, at a dose of 50mg once daily and increase by 50mg daily every 1-2 weeks. This again is based on a benefit versus risk assessment. The details of the initiation and titration regime will be communicated to the GP in all patients.

Missed dose:

If a dose is missed, the patient should be instructed to take the missed dose immediately, and then to take the next dose of lacosamide at the regularly scheduled time. If the patient notices the missed dose within 6 hours of the next dose, the patient should be instructed to wait to take the next dose of lacosamide at the regularly scheduled time. **Patient should not take a double dose.**

Elderly

No dose reduction is necessary in elderly patients. There is limited clinical data in elderly patients with epilepsy, particularly at doses greater than 400mg/day.

Renal impairment*:* No dose adjustment is necessary in mild and moderate renal impairment (CrCl >30ml/min).

In adult patients with mild or moderate renal impairment further dose titration >200 mg daily should be performed with caution.

In adult patients with severe renal impairment (CrCl ≤30ml/min) or with end-stage renal disease, a maximum dose of 250 mg/day is recommended and the dose titration should be performed with caution.

For all patients requiring haemodialysis a supplement of up to 50 % of the divided daily dose directly after the end of haemodialysis is recommended. Treatment of patients with end-stage renal disease should be made with caution as there is little clinical experience and accumulation of a metabolite (with no known pharmacological activity).

Hepatic impairment*:* A maximum dose of 300 mg/day is recommended for adult patients with mild to moderate hepatic impairment.

The dose titration in these patients should be performed with caution considering co-existing renal impairment. In patients weighing 50 kg or more, further dose titration > 200 mg daily should be performed with caution. The pharmacokinetics of lacosamide has not been evaluated in severely hepatic impaired patients should be administered to adult and paediatric patients with severe hepatic impairment only when the expected therapeutic benefits are anticipated to outweigh the possible risks. The dose may need to be adjusted while carefully observing disease activity and potential side effects in the patient.

Discontinuing treatment: If lacosamide has to be discontinued, it is recommended to taper the dose gradually (reducing the daily dose by 200mg/week).

In patients who develop serious cardiac arrhythmia, clinical benefit/risk assessment should be performed and if needed lacosamide should be discontinued.

Adverse Effects

Very common adverse effects that could occur include:

- Dizziness
- Headache
- Diplopia
- 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.

Common mild to moderate adverse effects can be managed by reducing lacosamide to the previously tolerated dose. This should be communicated to the Consultant or Specialist nurses via the contact details at the end of this document. Patients with a severe adverse drug reaction (e.g. angioedema) should be referred for immediate assessment in hospital.

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.

Contraindications

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

Special Warnings and Precautions for Use

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.

Pregnancy and Lactation

There is no adequate data from the use of lacosamide in pregnant women. 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.

Suicidal ideation and behaviour

Suicidal ideation and behaviour have been reported in patients treated with antiepileptic 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.

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. It also contains sorbitol, which may cause gastrointestinal discomfort and have a mild laxative effect.

For a full list of cautions, refer to the Summary of Product Characteristics for tablets or the Summary of Product Characteristics for syrup.

Drug Interactions

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

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.

For a full list of drug interactions, refer to the Summary of Product Characteristics.

Clinical Monitoring

No specific clinical monitoring needs to be undertaken. During general reviews with the patient, GPs should assess for seizure control and adverse effects of lacosamide, including signs of suicidal ideation and behaviours.

Preparations available

Tablets for oral administration*: 50mg, 100mg, 150mg and 200mg film-coated tablets.*

These tablets are film coated.

Oral suspension: 10mg/1ml (200ml total volume)

Lacosamide (Vimpat®) contains sodium. To be taken into consideration by patients on a controlled sodium diet.

Contact Details

National Hospital for Neurology and Neurosurgery (NHNN)	
NHNN Hospital Switchboard	020 3456 7890
NHNN Pharmacy Office	020 3448 3327
Epilepsy Nurse Specialists (answerphone)	020 3448 8627

References

1) Summary of Product Characteristics for Vimpat® UCB Pharma Limited last updated on eMC on the 10-Sept-2019 accessed via https://www.medicines.org.uk/emc/product/2278/ on 27/09/2019
2) Summary of Product Characteristics for Vimpat® UCB Pharma Limited last updated on eMC on the 10-Sept-2019 accessed via https://www.medicines.org.uk/emc/product/2285/ on 27/09/2019
3) British National Formulary. Edition 76. Last accessed via https://www.medicinescomplete.com/ on 01/05/2019