SHARED CARE GUIDELINE FOR LACOSAMIDE WHEN USED AS AN ADJUNCT TREATMENT OF EPILEPSY

INDICATION

Lacosamide is licensed for monotherapy and adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in adults, adolescents and children from 4 years of age with epilepsy.

NICE CG137 states that if first line anti-epileptic treatments are ineffective or not tolerated, tertiary epilepsy specialists may consider prescribing lacosamide as adjunctive treatment in children, young people and adults with:

- Refractory focal seizures
- Benign epilepsy with centrotemporal spikes, Panayiotopoulos syndrome or late-onset childhood occipital epilepsy (Gastaut type)

NICE CG137 does not cover use of lacosamide as monotherapy.

AREAS OF RESPONSIBILITY FOR SHARED CARE

Patients should be at the centre of any shared care arrangements. Individual patient information and a record of their preferences should accompany shared care prescribing guidelines, where appropriate.

Transfer of clinical responsibility to primary care should only be considered where the person’s clinical condition is stable or predictable.

Referral to the GP should only take place once the GP has agreed to this in each individual case, and the hospital or specialist will continue to provide prescriptions until a successful transfer of responsibilities. The GP should confirm the agreement and acceptance of the shared care prescribing arrangement and that supply arrangements have been finalised. The secondary/tertiary provider must supply an adequate amount of the medication to cover the transition period. The patient should then be informed to obtain further prescriptions from the GP.

When clinical responsibility for prescribing is transferred to general practice, it is important that the GP, or other primary care prescriber, is confident to prescribe the necessary medicines. Shared care agreements play a key role in enabling primary care prescribers to prescribe medicines with which they may not initially be familiar.

Clinical responsibility for prescribing is held by the person signing the prescription, who must also ensure adequate monitoring.

REFERRAL AND INITIATION

Shared Care is only appropriate if it provides the optimum solution for the patient.

### Specialist Responsibilities

<p>| | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>1</td>
<td>To assess the suitability of the patient for treatment with lacosamide, ensuring it is in line with the local and national recommendations.</td>
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<tr>
<td>2</td>
<td>Determine a management strategy and ensure follow-up in conjunction with the GP.</td>
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</table>
| 3 | Where appropriate:  
  • to initiate and stabilise the patient on treatment;  
  • clinically supervise patient by routine follow-up; |
### Specialist Responsibilities

- obtain consent from the patient’s GP to continue prescribing once treatment has been stabilised; the consultant will seek an agreement with the GP prior to agreeing a treatment plan with the patient;
- monitor the patient and their therapy at appropriate intervals (including bodyweight, and serum bicarbonate levels particularly in paediatric patients);
- ensure therapy is discontinued where applicable.

4. To explain the possible side effects of the medication to the patient and emphasise the importance of regular monitoring, where required

5. Ensure that patients know what to do and who to contact if they experience adverse events or an exacerbation of their condition.

6. To provide the GP with appropriate prescribing information and any additional information requested, and to offer telephone support.

7. To agree with the GP arrangements for any ongoing monitoring of the patient’s condition to ensure the safe use of lacosamide.

8. To be available for advice if the patient’s condition changes and to arrange follow up in clinic at intervals to monitor the progress of the disease and review the continued use of lacosamide.

9. To ensure that procedures are in place for the rapid re-referral of the patient by the GP.

10. To ensure the patient has given informed consent to their treatment.

11. To liaise with the GP on any suggested changes in prescribed therapy / notify GP of any changes in the patient’s condition as assessed on follow up.

12. To inform the GP when it is considered appropriate to discontinue treatment.


### General Practitioner Responsibilities

1. Initially, to refer the patient to the epilepsy specialist.

2. To prescribe lacosamide at the agreed dose after the initial 28-day period and monitor the patient’s ongoing response to lacosamide.

3. Carry out any agreed monitoring, reporting the results to the specialist if appropriate.

4. To deal with general health issues of the patient.

5. To liaise with the consultant regarding any complications or adverse effects of treatment.

6. To consider any side-effects reported by the patient and to discuss with the consultant if necessary.

7. To avoid or appropriately manage the drug interactions as listed below and in the current BNF.

8. To ensure ongoing reviews of the patient’s condition.

9. Ensure that therapy is discontinued where applicable.


### Patient's role (or that of carer)

1. Report to the specialist or GP if he/she does not have a clear understanding of the treatment.

2. Attend appropriate consultant and GP appointments.

3. Share any concerns in relation to treatment with lacosamide with their GP or consultant.

4. To report pregnancy or suspected pregnancy during treatment with lacosamide.
To seek help urgently from a healthcare professional if suspected side effects appear, or the patient is otherwise unwell.

**SUPPORTING INFORMATION**

**Dose, route of administration and duration of treatment**

Lacosamide must be taken twice a day (usually once in the morning and once in the evening).

Lacosamide may be taken with or without food.

**For adolescents and adults weighing 50kg or more**

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 at weekly intervals by 50 mg twice a day (100 mg/day), up to a maximum recommended daily dose of 400 mg (200 mg twice a day).

Lacosamide treatment may also be initiated with a single loading dose of 200 mg, followed approximately 12 hours later by a 100 mg twice a day (200 mg/day) maintenance dose regimen. Subsequent dose adjustments should be performed according to individual response and tolerability as described above.

**For children and adolescents weighing under 50kg**

The recommended starting dose is 2 mg/kg/day which should be increased to an initial therapeutic dose of 4 mg/kg/day after one week. Depending on response and tolerability, the maintenance dose can be further increased by 2 mg/kg/day every week. The dose should be gradually adjusted until the optimum response is obtained.

The following table summarises the recommended posology in adjunctive therapy for children and adolescents weighing less than 50 kg.

<table>
<thead>
<tr>
<th>Starting dose</th>
<th>2 mg/kg/day</th>
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<tbody>
<tr>
<td>Single loading dose</td>
<td>Not recommended</td>
</tr>
<tr>
<td>Titration (incremental steps)</td>
<td>2 mg/kg/day every week</td>
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<tr>
<td>Maximum recommended dose in patients &lt; 20 kg</td>
<td>up to 12 mg/kg/day</td>
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<tr>
<td>Maximum recommended dose in patients ≥ 20 kg to &lt; 30 kg</td>
<td>up to 10 mg/kg/day</td>
</tr>
<tr>
<td>Maximum recommended dose in patients ≥ 30 kg to &lt; 50 kg</td>
<td>up to 8 mg/kg/day</td>
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In accordance with current clinical practice, if lacosamide has to be discontinued, it is recommended this be done gradually (e.g. taper the daily dose by 200 mg/week).

**Adverse effects (incidence, identification, importance and management)**

*Common or very common*

Asthenia; concentration impaired; confusion; constipation; depression; diarrhoea; dizziness; drowsiness; dry mouth; dysarthria; dyspepsia; flatulence; gait abnormal; headache; insomnia; mood altered; movement disorders; muscle spasms; nausea; nystagmus; sensation abnormal; skin reactions; tinnitus; vertigo; vision disorders; vomiting

*Uncommon*

Aggression; agitation; angioedema; arrhythmias; atrioventricular block; hallucination; psychotic disorder; suicidal tendencies; syncope
Frequency not known
Agranulocytosis

Cautions and contra-indications

Contraindications
- Hypersensitivity to lacosamide.
- Known second- or third-degree atrioventricular (AV) block.
- Child aged under 4 years of age
- Breastfeeding

Special warnings
- 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.
- 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.
- Lacosamide should be used with caution in patients with known cardiac conduction problems, severe cardiac disease (e.g. history of myocardial infarction or heart failure), in elderly patients, or when lacosamide is used in combination with products known to be associated with PR prolongation. In these patients it should be considered to perform an ECG before a lacosamide dose increase above 400 mg/day and after lacosamide is titrated to steady-state.
- Second-degree or higher AV block has been reported in post-marketing experience. Atrial fibrillation or flutter have both 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 of 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 counselled to seek medical advice should any of these symptoms occur.
- No dose adjustment is necessary in mildly and moderately renally impaired adult and paediatric patients (CLCR > 30 ml/min). In paediatric patients weighing 50 kg or more and in adult 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 paediatric patients weighing 50 kg or more and in adult patients with severe renal impairment (CLCR ≤ 30 ml/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. If a loading dose is indicated, an initial dose of 100 mg followed by a 50 mg twice daily regimen for the first week should be used. In paediatric patients weighing less than 50 kg with severe renal impairment (CLCR ≤ 30 ml/min) and in those with end-stage renal disease, a reduction of 25 % of the maximum dose is recommended. 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).
- A maximum dose of 300 mg/day is recommended for paediatric patients weighing 50 kg or more and 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 adolescents and adults weighing 50 kg or more, a loading dose of 200 mg may be considered,
but further dose titration (> 200 mg daily) should be performed with caution. Based on data in adults, in paediatric patients weighing less than 50 kg with mild to moderate hepatic impairment, a reduction of 25 % of the maximum dose should be applied. The pharmacokinetics of lacosamide has not been evaluated in severely hepatic impaired patients (see section 5.2). Lacosamide 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.

- Treatment with lacosamide has been associated with dizziness which could increase the occurrence of accidental injury or falls. Patients should be advised to exercise caution, and not drive or operate machinery until they are familiar with the potential effects of the medicine.

**Monitoring requirements and responsibilities**

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

**Clinically important drug interactions and their management**

- Lacosamide should be used with caution in patients treated with medicinal products known to be associated with PR prolongation (e.g. carbamazepine, lamotrigine, eslicarbazepine, pregabalin) and in patients treated with class I antiarrhythmics.

- 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.

- 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. Lacosamide plasma concentrations were not affected by carbamazepine and by valproic acid. Population pharmacokinetic analyses in different age groups estimated that concomitant treatment with other antiepileptic medicinal products known to be enzyme inducers (carbamazepine, phenytoin, phenobarbital, in various doses) decreased the overall systemic exposure of lacosamide by 25 % in adults and 17 % in paediatric patients.

- 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.

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**This list is not exhaustive. The manufacturer’s summary of product characteristics (SPC) and the most current edition of the British National Formulary should be consulted for full information on contra-indications, warnings, side-effects and drug interactions.**

**Peer-reviewed references for product usage**

1. BNF online  
   [https://www.medicinescomplete.com](https://www.medicinescomplete.com)

2. Summary of product characteristics for Vimpat® (accessed 17/12/2018)
3. Drug tariff (December 2018)
   https://www.drugtariff.nhsbsa.nhs.uk/#/00667352-DB/DB00666980/PartVIIAproductsZ

4. NICE CG137: Epilepsies and their management (April 2018)
   https://www.nice.org.uk/Guidance/cg137

Contacts for more detailed information

<table>
<thead>
<tr>
<th>Contact Details</th>
<th>Telephone Number</th>
<th>Email</th>
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<tbody>
<tr>
<td>Consultant Neurologist: Dr R Page</td>
<td></td>
<td><a href="mailto:Rupert.Page@poole.nhs.uk">Rupert.Page@poole.nhs.uk</a></td>
</tr>
<tr>
<td>Epilepsy Specialist Nurses: Michelle Knight Cindy Sharland</td>
<td>01202 442231</td>
<td><a href="mailto:Michelle.Knight@poole.nhs.uk">Michelle.Knight@poole.nhs.uk</a> <a href="mailto:Cindy.Sharland@poole.nhs.uk">Cindy.Sharland@poole.nhs.uk</a></td>
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Drug costs

- Lacosamide 50mg capsules x 14 = £10.81
- Lacosamide 100mg capsules x 56 = £86.50
- Lacosamide 150mg capsules x 56 = £129.74
- Lacosamide 200mg capsules x 56 = £144.16
- Lacosamide oral solution 10mg/ml sugar free, 200ml = £25.74

Prices correct at 17 December 2018

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<thead>
<tr>
<th>Written By</th>
<th>Neurology working group</th>
<th>December 2018</th>
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<tbody>
<tr>
<td>Approved By</td>
<td>Dorset Medicines Advisory Group</td>
<td>January 2019</td>
</tr>
<tr>
<td>Date of next review</td>
<td>January 2021 or before, in light of new evidence or information.</td>
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