Lacosamide (Vimpat) for partial-onset epilepsy – monotherapy

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The National Horizon Scanning Centre Research Programme is part of the National Institute for Health Research
Lacosamide (Vimpat) for partial-onset epilepsy – monotherapy

Target group
- Epilepsy: partial onset myoclonic seizures – monotherapy.

Technology description
Lacosamide (Vimpat) is an anticonvulsant with a dual mode of action: selective enhancement of sodium channel inactivation, and modulation of CRMP-2 (collapsin response mediator protein-2)\(^1\). Inactivation of slow sodium channels may help normalise activation thresholds and decrease pathophysiological neuronal activity, thus controlling neuronal hyperexcitability and stabilising the neural network\(^1\). The modulation of CRMP-2 may prevent the aberrant synaptic connectivity and/or rearrangements seen in epilepsy, thus influencing the development or progression of this disorder\(^2\). Lacosamide is intended as a monotherapy for the treatment of partial-onset seizures. If licensed as a monotherapy, it will be administered orally at 200, 400, or 600mg daily.

Lacosamide is licensed as adjunctive therapy for the treatment of partial-onset seizures with or without secondary generalisation in patients with epilepsy aged 16 years and older. Lacosamide has completed a phase II clinical trial for primary generalised tonic-clonic seizures in patients with idiopathic generalised epilepsy. It is in phase II clinical trials for fibromyalgia and osteoarthritis.

The most common adverse effects (AEs) associated with lacosamide when used for its licensed indication include depression, confusional state, insomnia, dizziness, headache, balance disorder, abnormal coordination, memory impairment, cognitive disorder, somnolence, tremor, nystagmus, hypoesthesia, dysarthria, disturbance in attention, diplopia, blurred vision, vertigo, tinnitus, nausea, vomiting, constipation, flatulence, dyspepsia, dry mouth, pruritus, rash, muscle spasms, gait disturbance, asthenia, fatigue, irritability and falls.

Innovation and/or advantages
If licensed, lacosamide will offer an alternative monotherapy option for this patient group. Lacosamide may enhance the inactivation of slow sodium channels, with no effects on fast inactivation\(^1\). This ability to preferentially block the electrical activity of neurons that are chronically depolarised provides an alternative pharmacological pathway to traditional antiepileptic drugs (AEDs) such as carbamazepine and lamotrigine\(^2\).

Developer
UCB Pharma Ltd.

Availability, launch or marketing dates, and licensing plans
In phase III clinical trials.

NHS or Government priority area
This topic is relevant to the National Service Framework for Long-term (Neurological) Conditions (2005).

Relevant guidance
- NICE technology appraisal. Retigabine for the adjunctive treatment of partial onset seizures in epilepsy. July 2011\(^3\).
- NICE technology appraisal. The clinical effectiveness and cost effectiveness of newer drugs for epilepsy in adults. March 2004\(^4\).


Canadian Agency for Drugs and Technologies in Health. Pharmacological treatments in patients with epilepsy: guidelines. April 20117.

SIGN. Diagnosis and management of epilepsy in adults. 2003 (updated October 2005)8.

Clinical need and burden of disease
Epilepsy affects approximately 260,000 to 416,000 people in England and Wales (approximately 0.5% of the population), 55% of whom have partial-onset seizures8,a. The mortality risk in people with epilepsy, particularly those with more severe seizures, is 2-3 times higher than the general population due to sudden unexpected death in epilepsy (SUDEP), underlying pathology related to the condition, and accidents8,9. About 60% of patients develop epilepsy above the age of 16 years, and 20% do not develop their condition until age 65 years or older10.

It has been estimated that 70% of people with active epilepsy can control recurrent seizures with existing AED monotherapy, a large percentage of which suffer from treatment side-effects2,10. The remaining 20–30%, approximately 42,900-68,640 patients in England and Wales with partial-onset seizures, remain refractory to current treatment even after starting on a third or a fourth drug2,b. In 2009, there were 3,807 hospital admissions due to localisation-related (partial) seizures (ICD G40.0-G40.2) in England, equating to 17,913 bed days11.

Existing comparators and treatments
The aim of epilepsy treatment is to prevent the occurrence of seizures by maintaining an effective dose of one or more AEDs10,12. The current NICE clinical guideline recommends AED monotherapy where possible6. The majority of patients with a new diagnosis of partial-onset epilepsy would be started on carbamazepine or lamotrigineb. In those for whom rapid control is preferable (where enzyme induction is potentially problematic) levetiracetam may be usedb.

Other current first line pharmacological treatment options for partial-onset seizures in adults include13:
- Oxcarbazepine
- Sodium valproate
- Gabapentin
- Topiramate

Efficacy and safety

<table>
<thead>
<tr>
<th>Trial</th>
<th>NCT01243177, SP0993, 2010-019765-28; ≥16 years old; lacosamide; phase III.</th>
<th>NCT01465997 extension, SP0994, 2010-021238-74; ≥16 years old; lacosamide; phase III extension.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sponsor</td>
<td>UCB, Inc.</td>
<td>UCB, Inc.</td>
</tr>
<tr>
<td>Status</td>
<td>Ongoing.</td>
<td>Ongoing.</td>
</tr>
</tbody>
</table>

a Expert opinion.
**Source of information**
| Trial registry, manufacturer. | Trial registry, manufacturer. |

**Location**
| EU, Canada and Australia. | Unknown. |

**Design**
| Randomised, active-controlled. | Non-randomised. |

**Participants and schedule**
- n=878 (planned); ≥16 years old; epilepsy; partial-onset seizures; newly or recently diagnosed. Randomised to lacosamide 100mg, 200mg, 300mg, 400mg, 500mg, or 600mg/day, or carbamazepine-controlled release 200mg, 400mg, 600mg, 800mg, 1,000mg or 1,200mg/day, all administered orally, for up to 118 weeks.
- n=527 (planned); ≥16 years old; epilepsy; partial-onset seizures; newly or recently diagnosed; completed per protocol trial NCT01243177. Continued on lacosamide 100mg, 200mg, 300mg, 400mg, 500mg, or 600mg/day, or carbamazepine-controlled release 200mg, 400mg, 600mg, 800mg, 1,000mg or 1,200mg/day, all administered orally, for up to 3.5 years.

**Follow-up**
- Active treatment period 118 weeks; then eligible subjects were allowed to participate in extension study SP0994 (NCT01465997).
- Not known.

**Primary outcome**
- Proportion of subjects remaining seizure free for 6 consecutive months of treatment following stabilisation at the last evaluated dose for each subject.
- Proportion of subjects with ≥ 1 adverse events (AEs); proportion of subjects ≥ 1 serious AEs; withdrawal due to AEs.

**Secondary outcome**
- Proportion of subjects remaining seizure free for 12 consecutive months following stabilisation at the last evaluated dose for each subject.
- Not known.

**Expected reporting date**
- March 2014.
- December 2014.

**Estimated cost and cost impact**

The cost of lacosamide has not yet been determined for this indication. However, lacosamide for the adjunctive treatment of epilepsy in adult patients with partial-onset seizures costs £86.50 for 28 days at a dose of 100mg twice daily\(^{12}\). The cost of other selected monotherapy treatment options are\(^{12}\):

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose (maintenance therapy)</th>
<th>Cost per 28 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamazepine</td>
<td>400mg twice daily</td>
<td>£7.62</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>100mg twice daily</td>
<td>£4.00</td>
</tr>
<tr>
<td>Oxcarbazepine</td>
<td>600mg twice daily</td>
<td>£49.39</td>
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<tr>
<td>Sodium valproate</td>
<td>500mg twice daily</td>
<td>£5.20</td>
</tr>
<tr>
<td>Levetiracetan (Keppra)</td>
<td>500mg twice daily</td>
<td>£52.30</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>600mg three times daily</td>
<td>£17.91</td>
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<tr>
<td>Topiramate</td>
<td>100mg twice daily</td>
<td>£4.88</td>
</tr>
</tbody>
</table>

**Claimed or potential impact – speculative**

**Patients**
- Reduced mortality or increased length of survival
- Reduction in associated morbidity or improved quality of life for patients and/or carers
- Quicker, earlier or more accurate diagnosis or identification of disease
- None identified

**Services**
- Increased use
- Service organisation
- Staff requirements
- Decreased use
- Other:
- None identified
Costs

- Increased unit cost compared to alternative
- Increased costs: more patients coming for treatment
- Increased costs: capital investment needed
- New costs:
- Savings:
- Other:

Other issues

- Clinical uncertainty or other research question identified: None identified

References

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