An audit of the use of lacosamide in adult epilepsy: Is lacosamide being used safely, correctly and effectively?

Catherine James, Final Year Medical Student – Cardiff University

Introduction and objectives: Lacosamide was licensed in 2008 as 'adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in patients with epilepsy aged 16 years or over'. It is hoped that Lacosamide's novel mode of action, by enhancing entry of voltage gated sodium channels into the slow inactivation state, may both enhance outcomes and minimise synergistic side effects. All pharmacological intervention carries an inherent risk, and with a new drug in particular, it is vital to minimise potential harm by safe prescribing according to guidelines, and to optimise treatment through regular assessment of outcomes. This retrospective audit was carried out by a medical student at Cardiff University as a final year project.

The objectives were to:

- Research and devise a set of auditable standards and collect data about prescribing practices and outcomes
- Use these results to highlight areas of good practice and recommend changes to further optimise patient care
- Learn about issues surrounding prescribing for patients with epilepsy.

Setting and population: Patients with partial-onset seizures aged 16 or over who are currently prescribed or have been prescribed Lacosamide since 2009 at the Epilepsy Unit at University Hospital of Wales, Cardiff.

Methods: In order to establish the gold standards of prescribing and care, the Summary of Product Characteristics (SPC), published by the manufacturer UCB Pharma Ltd, was reviewed. A search of the literature using the databases EMBASE, Medline, Ovid Medline and PubMed was performed, using LACOSAMIDE and/or VIMPAT as key terms. Searches were limited to

English Language and studies published after 2000. The NICE database contained no guidelines published specifically for lacosamide, nor is it mentioned in Clinical Guideline 20 (2004) concerning the diagnosis and management of epilepsies. Patient information leaflets were sought and searching the library database with the keyword EPILEPSY identified textbooks. Patient clinic letters were accessed through the Clinical Portal System and data was collected using a proforma.

Results: 55 patients were included in this study. Not all standards are being met; there was <50% compliance for pre-treatment ECG, discussions about AV block and AF, discussions about teratogenicity and psychiatric monitoring. Poor documentation may partially explain these results. 44% of patients reported a decrease in seizure frequency, although as a retrospective study the change in seizures could not be quantified. 62% of patients reported at least one side effect; the most commonly experienced was dizziness. The discontinuation rate was 38%. Over 60% of patients were taking a VGSC blocker alongside lacosamide. Of these, 5 patients were taking 2 VGSC blockers. The discontinuation rate amongst this group of patients was 80%; side effects were reported as the main reason for discontinuation in these patients, and none of these patients reported a reduction is seizure frequency.

Conclusion: Despite some areas of poor compliance, the use of lacosamide was found to be safe and effective in this centre. It was clear that some of the initial standard setting was over-rigorous and new recommendations were made based upon the results and literature. Implementation of the recommendations will further improve prescribing practices of this new drug. Increased side-effects in patients on two concomitant voltage gated sodium channels (VGSC) blockers is an important finding that warrants further investigation.

Proforma for data collection-Lacosamide Audit

Demographics

1. Age:
2. Gender:
3. Seizure type: Partial onset / Generalised

Standards being audited:

4. Is it being used for focal epilepsy? Yes / No
5. Is an ECG being performed on at risk patients* before treatment started? Yes / No
6. Has the patient been made aware of the symptoms of heart block/ AF (if at risk*) Yes / No
7. A) Is the patient on other voltage gated sodium channel blocking AEDs? Yes / No

   B) Which VGSC blocker(s)? *Phenytoin / Carbamazepine / Lamotrigine / Pregabalin*
8. Is there documented evidence of discussion with women of childbearing potential about possible teratogenic effects? Yes / No
9. Is the patient being monitored for psychiatric side effects? Yes / No

Outcomes

1. Duration of therapy:
2. Reason for stopping (if applicable): *Side effects / No effect / Worsening seizures / Pregnancy / Other*
3. Seizure frequency on lacosamide: *Decreased / Increased / Same*
4. Side effects**: *Nervous system / Psychiatric / Eye / Ear / GI / General*

* These are patients with symptomatic heart block, history of cardiac problems, diabetes

** As classified by the UCB Pharma Summary of Product Characteristics:

System organ class	Side effects
Psychiatric Disorders	Depression, confusion, insomnia, aggression, agitation, psychosis, suicide attempt/ideation
Nervous system Disorders	Dizziness, headache, balance disorder, abnormal co-ordination, memory impairment, somnolence, tremor, nystagmus, dysarthria, hypoesthesia
Eye Disorders	Diplopia, blurred vision
Ear Disorders	Vertigo, tinnitus
GI Disorders	Nausea, vomiting, constipation, flatulence, dyspepsia
General Disorders	Fatigue, asthenia, gait disturbance, irritability, injection site pain

Modified standards based on original audit

Recommendation	Notes
All at-risk patients should have an ECG prior to treatment	These are patients with symptomatic heart block, history of cardiac problems, diabetes
At-risk patients must be told about symptoms of AV block and AF	At risk defined as above. Strongly recommended that all patients are warned
Exhibit caution in prescribing lacosamide to patients already on VGSC blockers (carbamazepine, lamotrigine, phenytoin and pregabalin)	Consider altering dose or concomitant medication to maximise the chance of the patient tolerating and experiencing positive effects
Women of childbearing potential **must** be told about unknown risks of teratogenicity in pregnancy	100% compliance is expected here. The discussion **must** be documented
All patients with epilepsy should be monitored for psychiatric co-morbidity, especially so with a new drug	All members of the multidisciplinary team should be involved
Lacosamide should be used for partial onset seizures but may be used in generalised seizures	If used outside license, must be in best interests of patients, have adequate follow up and be fully documented
Regular assessment of efficacy and side effects should be continued	This current practice is providing good results and should continue