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Lacosamide in Palliative Care: A Case Series

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Abstract

Neuropathic pain is a common and often challenging symptom in palliative care. Lacosamide has recently emerged as an unlicensed option for managing refractory neuropathic pain. This case series explores the use of lacosamide in four patients who were admitted to a hospice for symptom management. Whilst a potential analgesic benefit was observed in some cases, treatment was limited by adverse effects possibly associated with lacosamide, requiring dose reduction or discontinuation. These cases support the recommendation that lacosamide should be used as a second-line adjuvant for refractory neuropathic pain with gradual dose titration. Furthermore, they highlight the challenges in assessing lacosamide tolerability in palliative care, as there can often be an overlap between lacosamide-related adverse effects and symptoms of underlying pathology or alternative medication adverse effects. This can contribute to diagnostic overshadowing in clinical practice, delaying timely diagnosis and management of lacosamide-related adverse effects.

Categories: Pain Management, Palliative Care, Pharmacology
Keywords: analgesia, lacosamide, neuropathic pain, palliative care, side effects

Introduction

Complex pain management is a core aspect of palliative care practice, with neuropathic pain affecting up to 40% of cancer patients [1]. Cancer-related neuropathic pain can arise through several different pathways, including localised tumour invasion and compression of neural structures, treatment-related neurotoxicity, or iatrogenic nerve injury following surgical intervention. Cancer pain management is often further complicated by disease progression, organ dysfunction, and polypharmacy.

The Palliative Care Formulary suggests that the first-line agents for the management of neuropathic pain in palliative care include commencing either an antidepressant or a gabapentinoid antiepileptic as single therapy [2]. If pain remains sub-optimally managed, step two involves combining an antidepressant with a gabapentinoid antiepileptic. As a subsequent treatment option, lacosamide may be considered as an unlicensed, second-line adjunct for refractory neuropathic pain in palliative care when these medications are poorly tolerated or provide inadequate pain control.

Lacosamide is an antiepileptic drug, currently licensed as monotherapy and adjunctive treatment of focal seizures with or without secondary generalisation, as well as adjunctive treatment of primary generalised tonic-clonic seizures in children and adults [3,4]. Off-label uses include the management of status epilepticus, painful diabetic neuropathy and neuropathic pain [2,4].

The mechanism of action makes lacosamide particularly valuable in the management of refractory neuropathic pain, due to its ability to promote slow inactivation of voltage-gated sodium channels, thereby preferentially inhibiting rapidly firing neurones resistant to conventional sodium-channel blockers [2,5]. Additionally, given its mechanism of action, lacosamide may have a role in reducing opioid-induced hyperalgesia and improving opioid tolerability. This is because opioids' effects on voltage-gated sodium channels are thought to contribute to the pathophysiology of opioid-induced hyperalgesia, potentially resulting in tolerance and an increased risk of opioid toxicity [6]. However, further clinical trials are required to establish its efficacy in this context.

This case series describes clinical experiences of lacosamide use in palliative medicine, contributing to the emerging evidence base in this setting. This was a retrospective review of routine clinical practice. Inpatients prescribed lacosamide between November 2025 and January 2026 in a hospice inpatient unit were identified, and four patients were included. Electronic patient records were reviewed for patient demographics, diagnosis, pain description, functional impact of pain, adjuvant medications, lacosamide dosing and titration, effect on pain, and adverse effects. Outcomes were classified as treatment continuation or discontinuation. No interventions were made for research purposes.

Given the retrospective nature of this review, standardised pain assessment scores, for example, the Visual Analogue Scale or Numerical Rating Scale, were not consistently available in the electronic patient records. As such, evaluation of analgesic response and tolerability was based on the documentation of clinicians' descriptive assessments in the clinical notes.

Case Presentation

Case 1

A female patient in her 80s with metastatic lung cancer described intermittent burning pain radiating from her right shoulder to the fingertips, which was felt to be caused by possible brachial plexus involvement. Previously trialled analgesia included regular paracetamol 1000 mg four times a day, a buprenorphine 5 µg/hour patch, pregabalin 25 mg twice a day, amitriptyline 10 mg at night, and as-needed (*pro re nata* (PRN)) oral immediate-release morphine 5 mg, but these were all minimally effective or poorly tolerated and therefore stopped.

Oral lacosamide was initiated as the next-line analgesia in the community at 100 mg twice a day, alongside cyclizine for nausea. The patient subsequently developed new drowsiness and confusion. On hospice admission, cyclizine was suspected as the cause of her symptoms and was therefore discontinued, while lacosamide was increased to 150 mg twice a day for uncontrolled pain. The patient reported improved pain control and objectively appeared more comfortable; however, there was observed worsening of her cognition. As no other reversible cause was identified, lacosamide was stopped, following which her cognition improved but her pain escalated.

Lacosamide was later reintroduced at a lower dose of 50 mg at night, shortly after regular modified-release oxycodone 15 mg twice a day had been commenced. There were no adverse effects reported; therefore, the lacosamide dose was cautiously increased to 50 mg twice a day after five days with reported good effect. This resulted in treatment continuation. Figure *1* illustrates the timeline of events.

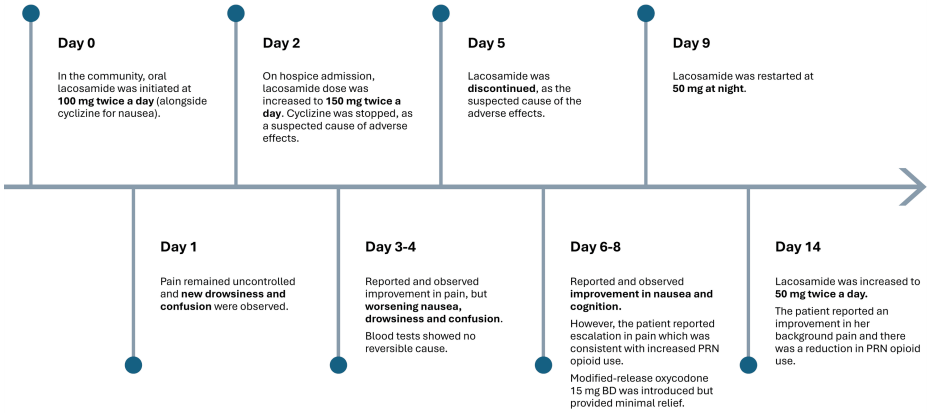


FIGURE 1: Timeline of lacosamide initiation, dose titration, effect on pain, and emergence of adverse effects in Case 1.

PRN: *pro re nata* (as needed); BD: *bis in die* (twice a day)

Case 2

A male patient in his 40s was diagnosed with anal squamous cell carcinoma with groin lymph node involvement and recurrent groin wound infections. CT imaging demonstrated disease progression, with a necrotic groin mass encasing the femoral neurovascular bundle (Figure *2*). This resulted in a severe throbbing ache in the right thigh, with a sharp pain radiating down the right leg. This pain was escalating despite regular paracetamol 1000 mg four times a day, ibuprofen 400 mg four times a day, pregabalin 300 mg twice a day, modified-release oxycodone 30 mg twice a day, and dexamethasone 8 mg once a day. The patient also frequently used PRN oral immediate-release oxycodone 15 mg and buccal fentanyl 200 µg.

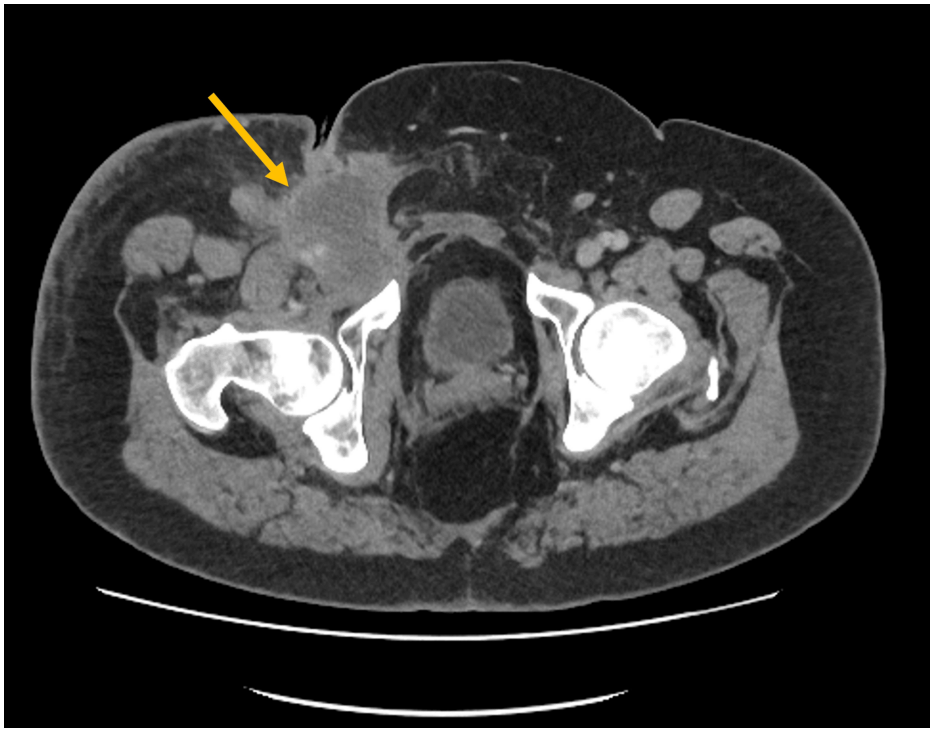


FIGURE 2: CT abdomen and pelvis showing the necrotic groin mass.

Oral lacosamide was therefore initiated shortly before hospice admission at 50 mg twice a day and titrated to 200 mg twice a day over 17 days, as demonstrated in Figure *3*. After four weeks of treatment at the maximum dose of lacosamide, the patient developed drowsiness, cognitive disturbance, hallucinations, diplopia, upper limb myoclonus and involuntary jaw movements. Due to suspicion of medication side effects, both lacosamide and oxycodone doses were reduced, after which these symptoms improved. Thereafter, lacosamide was gradually weaned and eventually discontinued following discharge from the hospice.

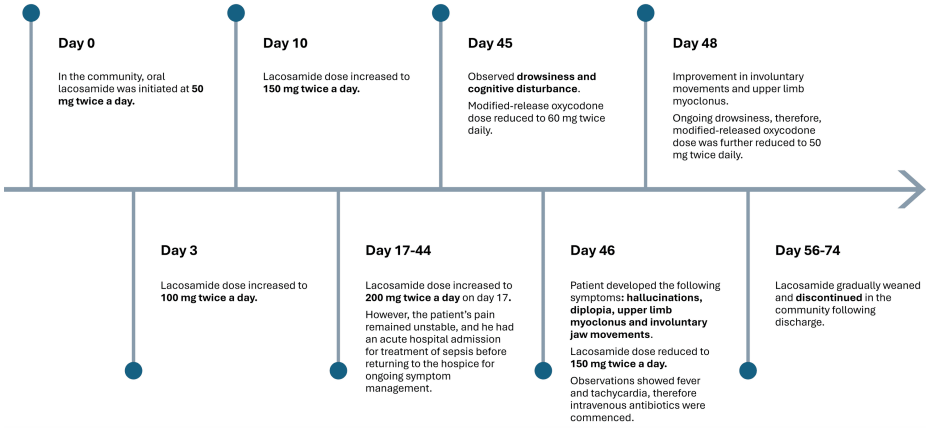


FIGURE 3: Timeline of lacosamide initiation, dose titration, effect on pain, and emergence of adverse effects in Case 2.

Assessment of lacosamide effectiveness and tolerability in this patient was complicated by recurrent wound infections and rapidly progressive disease, which exacerbated pain, frequent medication changes, and polypharmacy. Additionally, the high usage of PRN opioids blurred the distinction between opioid toxicity and lacosamide-related adverse effects.

Case 3

A female patient in her 80s with metastatic breast cancer, spinal metastases and an L1 pathological fracture was admitted to hospital with back pain limiting her mobility, confusion and word-finding difficulties. She

received radiotherapy for metastatic spinal cord compression, alongside correction of hypercalcaemia (serum adjusted calcium 3.05 mmol/L). Dexamethasone and gabapentin were trialled to optimise ongoing back pain but were later stopped due to poor tolerability. Oral lacosamide was then commenced at 50 mg twice a day and increased to 100 mg twice a day after two days.

On admission to the hospice, she reported improved pain control. This may have been attributable, at least in part, to radiotherapy and correction of hypercalcaemia, making it difficult to determine the extent to which lacosamide provided additional analgesic benefit. However, her confusion and word-finding difficulties persisted despite normalisation of her serum-adjusted calcium level, and no other reversible causes were identified. This prompted consideration of lacosamide adverse effects. Consequently, the lacosamide dose was reduced on day six and later discontinued, following which an improvement in her cognitive function was observed. Figure *4* illustrates the timeline of these events. The patient reported that her pain remained adequately controlled and her mobility returned to her baseline.

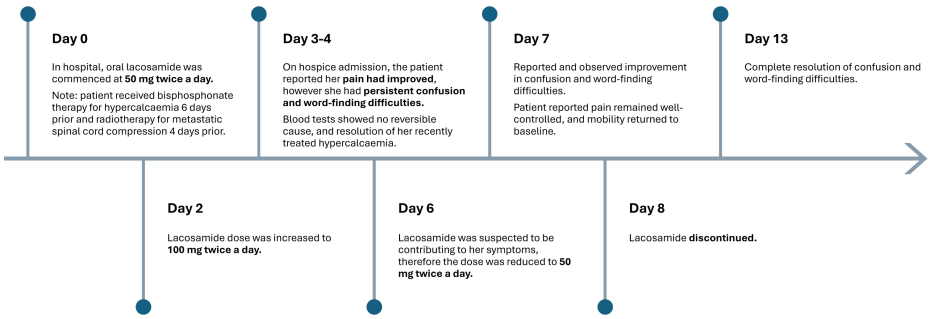


FIGURE 4: Timeline of lacosamide initiation, dose titration, effect on pain, and emergence of adverse effects in Case 3.

Case 4

A female patient in her 80s with metastatic rectal adenocarcinoma reported rectal pain and tenesmus. Regular paracetamol 1000 mg four times a day, a buprenorphine 5 µg/hour patch, and PRN ibuprofen 400 mg provided suboptimal pain relief.

Oral lacosamide was commenced in the community at 50 mg twice a day and titrated over one week to 200 mg twice a day, as seen in Figure *5*. The rationale for choosing lacosamide as the first-line neuropathic adjuvant is unclear from the clinical documentation. Initial titration was well tolerated and her pain improved. However, after four days at the maximum dose, she developed nausea, drowsiness, and impaired balance and coordination, which she described as resembling a Parkinsonian gait.

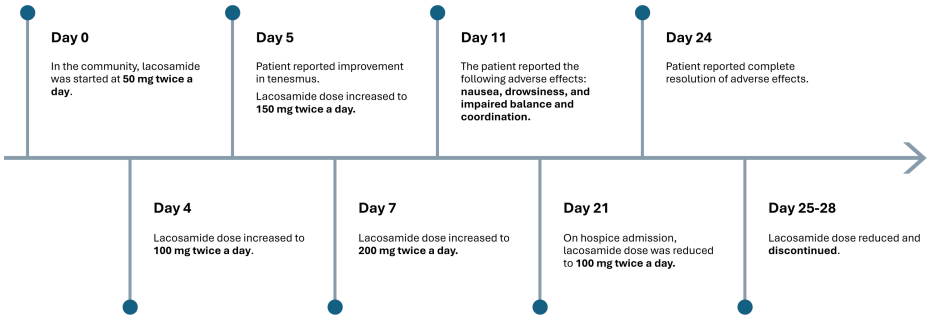


FIGURE 5: Timeline of lacosamide initiation, dose titration, effect on pain, and emergence of adverse effects in Case 4.

On hospice admission, lacosamide was suspected as the cause of her symptoms and was therefore gradually tapered and discontinued. Regular pregabalin, modified-release oxycodone and celecoxib (switched from ibuprofen) were up-titrated in the interim. Following these medication changes, the clinical notes documented sustained pain control and complete resolution of adverse effects.

Summary

Table 1 summarises the four cases, including their key clinical features, pharmacological management and treatment outcomes.

Patient demographics	Diagnosis	Pain description	Functional impact of pain	Other medications	Lacosamide dose titration	Effect on pain	Adverse effects	Possible confounding variables	Treatment outcome
Female in 80s	Metastatic lung cancer	Site: right upper limb pain. Onset: started 2.5 months ago Characteristics: intermittent burning pain radiating from shoulder to fingertips. Severity: not quantified using a standardised pain assessment score.	As the patient was right-hand dominant, pain affected their ability to independently manage their ADLs.	Previously trialled analgesia: paracetamol 1000 mg QDS (minimal relief), buprenorphine 5 micrograms/hour patch (minimal relief), pregabalin 25 mg BD (unsteadiness and confusion), amitriptyline 10 mg ON (drowsiness), and PRN oral immediate-release morphine 5 mg (ineffective). Patient was not on any regular analgesics when lacosamide was commenced.	Day 0: started at 100 mg BD; Day 2: increased to 150 mg BD; Day 5: discontinued; Day 9: restarted at 50 mg ON; Day 14: increased to 50 mg BD	After the dose was increased to 150 mg BD, patient reported improvement in pain and objectively appeared more comfortable on physical assessment. PRN opioid requirement increased after stopping lacosamide. After modified-release oxycodone was commenced and lacosamide was restarted, patient reported an improvement in her background pain which was consistent with a reduction in PRN opioid use.	Worsening nausea, drowsiness and confusion observed on days 1-4 of lacosamide dose titration. Patient reported an improvement in adverse effects following lacosamide discontinuation.	Cyclizine was commenced at the same time as lacosamide to help with nausea, and this may have contributed to drowsiness. Lacosamide was restarted soon after the introduction of modified-release oxycodone, and so the efficacy of lacosamide in particular is difficult to assess despite overall improvement in pain.	Continuation of lacosamide
Male in 40s	Anal squamous cell carcinoma with groin lymph node involvement and a necrotic groin mass encasing the femoral neurovascular bundle. Recurrent groin wound infections requiring treatment with intravenous antibiotics.	Site: right lower limb pain. Onset: not documented. Characteristics: constant throbbing ache in right thigh and intermittent sharp stabbing pain radiating down the right leg. Severity: NRS score 7/10 on hospice admission, but not routinely quantified using a standardised pain assessment score thereafter.	Remained independent with ADLs, however pain limited mobility.	Concurrent analgesia: paracetamol 1000 mg QDS, ibuprofen 400 mg QDS, pregabalin 300 mg BD, modified-release oxycodone 30 mg BD, dexamethasone 8 mg OD, PRN oral immediate-release oxycodone 15 mg, and PRN buccal fentanyl 200 micrograms.	Day 0: started at 50 mg BD; Day 3: increased to 100 mg BD; Day 10: increased to 150 mg BD; Day 17: increased to 200 mg BD; Day 46: reduced to 150 mg BD; Day 56-74: gradually weaned and discontinued.	The patient reported that he was unsure whether lacosamide was beneficial in managing his pain. His pain remained unstable with consistent high PRN opioid requirements and concomitant analgesic changes.	The following adverse effects were observed after four weeks of treatment at the maximum dose of lacosamide: drowsiness, cognitive disturbance, hallucinations, diplopia, upper limb myoclonus and involuntary jaw movements.	Polypharmacy, frequent medication changes and high usage of PRN opioids led to difficulty attributing adverse effects to lacosamide alone. Modified-release oxycodone was also reduced a day before lacosamide was reduced. The improvement in symptoms that followed therefore cannot be clearly attributed to lacosamide dose reduction. Recurrent groin wound infections and rapidly progressive disease were both likely exacerbating pain. This hindered assessment of analgesic efficacy of lacosamide.	Discontinuation of lacosamide
Female in 80s	Metastatic breast cancer with spinal metastases and an L1 pathological fracture. Metastatic spinal cord compression Hypercalcaemia (3.05 mmol/L)	Site: back pain. Onset: chronic lower back pain, with acute worsening over two days. Characteristics: constant dull ache with sharp, stabbing exacerbations on movement. Severity: not quantified using a	Pain affected mobility - patient could previously walk with a frame but due to pain, required assistance of one to mobilise even short	Previously trialled analgesia: dexamethasone 8 mg BD (night terrors) and gabapentin 200 mg TDS (myoclonic jerks). Patient was not on any regular analgesics when lacosamide was commenced.	Day 0: started at 50 mg BD; Day 2: increased to 100 mg BD; Day 6: reduced to 50 mg BD; Day 8: discontinued	Patient reported an improvement in pain, and her mobility improved back to her baseline (mobilising with a frame). No observation of a clear change in the pattern of PRN analgesic requirements.	Patient was acutely confused prior to lacosamide introduction. Hypercalcaemia was identified and treated. However, her confusion and word-finding difficulties persisted. One day following a lacosamide dose reduction, an improvement in her confusion and word-finding difficulties was reported. Complete	Radiotherapy for metastatic spinal cord compression and correction of hypercalcaemia may have both contributed to the improvement in her pain.	Discontinuation of lacosamide

		standardised pain assessment score.	distances.				resolution of her symptoms was reported 5 days following lacosamide discontinuation.		
Female in 80s	Metastatic rectal adenocarcinoma	Site: rectal pain. Onset: not clearly documented. Characteristics: patient described tenesmus and "red hot pokers in her anus". Severity: not quantified using a standardised pain assessment score.	Remained independent with ADLs.	Concurrent analgesia: paracetamol 1000 mg QDS, buprenorphine 5 micrograms/hour patch, and PRN ibuprofen 400 mg.	Day 0: started at 50 mg BD; Day 4: increased to 100 mg BD; Day 5: increased to 150 mg BD; Day 7: increased to 200 mg BD; Day 21: reduced to 100 mg BD; Day 25-28: weaned and discontinued	Patient reported improvement in tenesmus and rectal pain following the introduction of lacosamide. No clear report of any changes in the pattern of PRN analgesic requirements. PRN ibuprofen was switched to regular celecoxib after lacosamide had been titrated to maximum dose with which patient had already reported an improvement in her pain. Whilst lacosamide was being weaned, the buprenorphine patch was discontinued and regular pregabalin and modified-release oxycodone were introduced and up-titrated to maintain pain control.	The following adverse effects were observed after four days of treatment at the maximum dose of lacosamide (day 11): nausea, drowsiness, and impaired balance and coordination (patient described as resembling a Parkinsonian gait). Complete resolution of adverse effects was reported three days following lacosamide dose reduction.	No obvious confounders identified.	Discontinuation of lacosamide

TABLE 1: Summary of patient demographics, diagnosis, pain description, functional impact of pain, other medications, lacosamide dose titration, effect on pain, adverse effects, possible confounding variables, and treatment outcome in all four cases.

ADLs: activities of daily living; PRN: *pro re nata* (as needed); BD: *bis in die* (twice a day); L1: first lumbar vertebra; NRS: numeric rating scale; ON: *omni nocte* (at night); QDS: *quater die sumendum* (four times a day); TDS: *ter die sumendus* (three times a day).

Discussion

Neuropathic pain represents a significant challenge in palliative medicine, particularly when refractory to conventional analgesics. Lacosamide is a relatively underexplored option, with the current evidence base limited by small sample sizes and a lack of controlled studies in the palliative care setting. Nevertheless, emerging evidence suggests a potential role for its use. A chart review of lacosamide in palliative care reported that pain improved significantly in 35% of patients, with the drug generally well tolerated and straightforwardly converted between oral and subcutaneous administration [7].

The availability of lacosamide as a subcutaneous formulation offers a practical advantage for patients in whom impaired gastrointestinal absorption, persistent nausea and vomiting, or dysphagia limit the use of oral medications. A published letter describes a case example of effective parenteral lacosamide use in the management of refractory neuropathic pain, with a 1:1 ratio when converting from the subcutaneous to oral formulation [5].

The use of lacosamide may, however, be limited by associated adverse effects including cognitive impairment, drowsiness, nausea, and movement disorders [3]. Similar side effects were observed in the present case series, which led to treatment discontinuation in three of the four patients.

One hypothesis is that the poor tolerability of lacosamide observed in these cases may, in part, be attributable to rapid dose titration. In all four cases, the rate of titration exceeded that recommended by the Palliative Care Formulary, which advises initiating at 50 mg twice a day and increasing by 50 mg twice a day at weekly intervals [2]. In contrast, Crispin and Jenks report subcutaneous dose increments of 50 mg per 24 hours every three to four days, which is a comparable rate to the above recommendation, and this was reportedly well tolerated without adverse effects [5].

Furthermore, patients are often commenced on concomitant analgesics, particularly opioids, for pain management in palliative care. These analgesics can have similar side effects to lacosamide, such as drowsiness and nausea; therefore, attributing these symptoms to a single agent may be challenging [8]. This can complicate the overall assessment of lacosamide tolerability.

Additionally, underlying pathologies, such as intracranial malignancies, may present with neurological

symptoms that overlap with known adverse effects of lacosamide, including confusion and tremors [3]. This similarity in clinical presentation may increase the risk of diagnostic overshadowing, whereby clinicians familiar with these symptoms as manifestations of the underlying pathology may attribute them solely to the disease and fail to recognise a potential contribution from lacosamide. Careful evaluation of the temporal relationship between treatment initiation, dose escalation and onset of adverse effects is therefore essential.

Several limitations should be considered when interpreting the findings of this case series. Firstly, the small sample size limits the generalisability of findings. Secondly, the retrospective design hindered the use of standardised pain assessment scores. Analgesic response was instead assessed using qualitative documentation in clinical notes rather than validated quantitative measures of pain intensity, limiting objective assessment and comparison of analgesic outcomes. Additionally, with the absence of a control group, the findings are subject to potential confounding. Symptoms associated with advanced disease, concurrent infection, and side effects of concomitant medications may overlap with those attributable to lacosamide, making it difficult to isolate lacosamide as the sole cause. Equally, adjuvant analgesics and concurrent interventions, such as radiotherapy and correction of electrolyte abnormalities, can contribute to improvement in pain, complicating the assessment of lacosamide efficacy. Therefore, although this case series provides a descriptive account of clinical observations, it cannot establish a causal relationship between lacosamide and the observed efficacy or adverse effects. Nevertheless, this report highlights the potential benefit of lacosamide as an adjunct in the management of complex neuropathic pain in palliative care. Further research is needed to establish its role in this setting.

Conclusions

This case series reflects real-world prescribing in a complex population with significant symptom burden, multimorbidity, and polypharmacy. A possible improvement in neuropathic pain with lacosamide use was observed, suggesting its potential role in managing refractory neuropathic pain within palliative medicine. However, the tolerability of lacosamide may be limited by its side-effect profile, although the contribution of rapid dose titration and concomitant use of analgesics remains uncertain. The observations in this case series are consistent with the recommendation of considering lacosamide as a second-line adjuvant and support consideration of a slower dose-titration regimen. This could perhaps improve tolerability and enable treatment continuation. Finally, it is imperative for clinicians to remain vigilant for lacosamide-related adverse effects, particularly when symptoms can often overlap with those of the underlying disease and concomitant medications.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Luxshini Selvarajah, Cecily Bloom

Acquisition, analysis, or interpretation of data: Luxshini Selvarajah, Cecily Bloom

Drafting of the manuscript: Luxshini Selvarajah, Cecily Bloom

Critical review of the manuscript for important intellectual content: Luxshini Selvarajah, Cecily Bloom

Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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Cecily Bloom and Luxshini Selvarajah contributed equally to the work and should be considered co-first authors.

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