Journal of Pain Research

Dovepress
Taylor & Francis Group

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LETTER

Ziconotide as an Opioid Rescue: Economic, Clinical, and Subgroup Considerations [Letter]

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Dear editor

We read with great interest the exploratory study by Canovas Martínez et al, which provides preliminary evidence supporting intrathecal ziconotide as an opioid rescue strategy in patients with refractory chronic pain.[1] The observed reductions in morphine dosage, pain intensity (VAS 8.0 to 2.5), and neuropathic symptoms (DN4 6.0 to 2.0), achieved without notable adverse events, underscore ziconotide's potential to mitigate opioid-related toxicities such as tolerance and endocrine dysfunction. This small cohort study therefore contributes to the growing evidence for non-opioid alternatives in intrathecal therapy and highlights the urgent need for opioid-sparing approaches amid the ongoing opioid crisis. Nevertheless, translating these findings into clinical practice requires addressing several critical challenges.

One major barrier is cost and accessibility. Ziconotide's high price—estimated at £395,748 for first-year combination therapy compared with £136,628 for morphine monotherapy in cancer pain—may limit widespread adoption, particularly in resource-constrained settings.[2] A budget impact analysis by Lambe et al demonstrated that while incorporating ziconotide increases short-term expenditures, it may generate long-term savings by reducing opioid-related complications, underscoring the importance of cost-effectiveness analyses across diverse healthcare systems.[3] Consequently, future multicenter studies should integrate health economic modeling to better define its value proposition and inform reimbursement decisions.

Beyond economic considerations, optimization of dose titration strategies also warrants further study. The authors' slow titration protocol (0.5 μg weekly increments) successfully minimized adverse events, consistent with expert recommendations to start at 0.5–1.2 μg/day and escalate by no more than 0.5 μg/day. However, comparative trials are necessary to evaluate faster versus slower titration schedules. For example, a randomized controlled trial by Rauck et al showed that gradual titration improved tolerability and allowed higher effective doses without psychiatric adverse effects.[4] Such head-to-head assessments could refine titration protocols, ensuring an optimal balance of efficacy, safety, and adherence.

Equally important is the evaluation of ziconotide in specific patient subgroups. The current cohort (ages 53–75 years) excluded younger adults, who may derive greater benefit given their lower risk of opioid-induced hypogonadism and tolerance. In addition, consensus guidelines by Deer et al recommend cautious use in patients with psychiatric or cardiopulmonary comorbidities, highlighting the need for stratified analyses in both younger populations and those with cancer-related pain.[5] Subgroup-specific trials would help identify likely responders, refine indications, and define contraindications.

In conclusion, this exploratory study positions ziconotide as a promising opioid-sparing therapy. To fully establish its clinical role, larger multicenter randomized trials are required, incorporating economic analyses, titration strategy evaluations, and subgroup-specific assessments. Addressing these dimensions will be essential to translate early promise into meaningful clinical practice.

Received: 3 October 2025
Accepted: 29 October 2025
Published: 7 November 2025

Funding

There is no funding to report.

Disclosure

The authors declare that they have no competing interests in this communication.

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https://doi.org/10.2147/JPR.S571927