

Ziconotide in Complex Regional Pain Syndrome

by Lynn R. Webster, MD, FACPM, FASAM

Ziconotide is a novel medication developed from marine life. It is a synthesized peptide component of a neurotoxin secreted by the cone shell snail, *Conus magus*, which is thought to work by preventing the release of neurotransmitters involved in the transmission of pain at the spinal cord level. Ziconotide was recently approved by the U.S. Food and Drug Administration (FDA) for the treatment of chronic severe pain in which intrathecal (IT) therapy is warranted. In IT therapy, medication is delivered by catheter to the spinal fluid by means of an internal pump implanted in the abdomen.

Candidates for IT therapy are people with moderate-to-severe pain who failed systemic medication therapy or experienced intolerable side effects due to oral medications. To be considered for ziconotide therapy, it is important that patients have realistic expectations regarding treatment of their pain and have complied with past treatments. Some therapeutic goals of IT therapy include achieving greater than 50% pain relief, reduction of side effects, and improvement in patient quality of life and function.

Ziconotide has not been formally studied in patients only with complex regional pain syndrome (CRPS/RSD); however, its safety and efficacy have been evaluated in three double-blind, placebo-controlled studies, and four long-term, open-label studies. A review of these studies found 17 people who participated in clinical trials had a diagnosis of CRPS/RSD; 11 patients received ziconotide, and six received placebo. The mean change in the Visual Analog Scale of Pain Intensity (VASPI) for this subset of patients was 25.2% for patients who received ziconotide and 2.8% for placebo.

Case Study Demonstrates Relief

In review of literature, one case report demonstrated the benefit of ziconotide in a 16-year-old male with CRPS/RSD involving bilateral lower extremities who had failed standard care for CRPS/RSD. He received ziconotide in ranges from 2.5 mcg/day to 7.6 mcg/day for a reported duration of three years. Initial response was improvement in pain reported at six weeks on 5.5 mcg/day. The patient

achieved normal gait at seven months of therapy at a dose of 6.5 mcg/day. The dose was then reduced to 2.8 mcg/day, and the patient reported complete resolution of his pain after three years of therapy with ziconotide. He experienced the side effects of urinary retention and depression while treated with ziconotide.

Ziconotide is generally well tolerated if it is started at a low dose of ≤ 1 mcg/day and titrated ≤ 0.5 mcg/day at no greater than weekly intervals. Common side effects reported in greater than 25% of patients in clinical studies include dizziness, nausea, confusion, headache, nystagmus, and abnormal sensations. It is important to note that the starting dose and titration rate were greater than recommended above. Side effects can be managed by dose reduction or cessation of therapy. Ziconotide can be stopped abruptly without any signs of withdrawal.

Although ziconotide is FDA approved for monotherapy, the treating physician may choose to use it in combination with other medications in the pump. This would not deviate from standard of practice. Ziconotide may prove additive or synergistic when combined with other medications in pump.

Ziconotide is a novel medication in the armamentarium to combat moderate-to-severe chronic pain. A review of clinical trial data and scientific literature shows that ziconotide may benefit patients with CRPS/RSD who have failed standard therapies. Responsible use of ziconotide will ensure its success. However, it is important to manage both physician and patient expectations; at the recommended starting dose and titration, it may take a few months to reach therapeutic benefit. As demonstrated above in the case report, maximum benefit was not achieved for several months, and immediate gratification should not be expected.

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