Molina Clinical Policy
Prialt (ziconotide intrathecal infusion): Policy No. 387

Last Approval: 10/09/2024
Next Review Due By: October 2025

DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment, and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a Member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid Members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

OVERVIEW

Prialt [ziconotide intrathecal infusion] is an N-type calcium channel blocker nonopioid analgesic that works by targeting and blocking calcium channels on nerves that transmit pain signals to the brain. Neuropsychiatric symptoms such as depression, cognitive impairment, and hallucinations; decreased levels of consciousness; and an increase in creatine kinase levels are among ziconotide-related adverse events. Ziconotide is also associated to a risk of meningitis due to possible contamination of the intrathecal device. Due to its limited therapeutic window, ziconotide must be dosed with care (Smith et al. 2009). Intrathecal administration of lower dosages of ziconotide reduces systemic toxicity. Long-term administration of intravenous ziconotide does not appear to induce tolerance and has no effect on morphine analgesia or opiate-analgesia tolerance. However, due to the potential for serious neurologic and psychiatric side effects, its use should be restricted to patients who have not responded to other therapies, and it is recommended that only clinicians and physicians experienced in the use of intrathecal medication therapy should administer ziconotide.

Ziconotide, unlike morphine, does not bind to opioid receptors and is not inhibited by opioid antagonists, as a result, Ziconotide provides an alternative to morphine for pain specialists to avoid opioid-related respiratory depression in patients with lung disease, compromised respiratory reserve, or peripheral edema, and in patients with opioid resistance who require high doses or rapidly escalating doses, or who develop opioid-induced hyperalgesia. Ziconotide is not associated with tolerance, withdrawal, or granulomas, and has may lead to a decrease in oral opioid intake in patients with complex regional pain syndrome (Herring et al. 2019).

Regulatory Status

Prialt was FDA approved in December 2004 for the indication of “for the management of severe chronic pain in patients for whom intrathecal (IT) therapy is warranted, and who are intolerant of or refractory to other treatment, such as systemic analgesics, adjunctive therapies or IT morphine”. Despite the adverse events experienced by patients, the FDA approval letter indicates the benefits of ziconotide intrathecal medication therapy outweighs the negative patient experience (FDA 2004).

COVERAGE POLICY

Prialt [ziconotide intrathecal infusion] for the management of severe chronic pain **may be considered medically necessary** when **ALL** the following clinical criteria are met:

1. Member is age 18 or older
2. Prescribed by, or under the supervision of, a pain management specialist (e.g., neurologist, anesthesiologist) experienced in the technique of intrathecal administration and familiar with the drug and device labeling
3. Diagnosis of severe, chronic pain for which intrathecal therapy is warranted
4. Evaluation by a licensed behavioral and/or mental health care provider to rule out pre-existing history of

psychosis, current psychiatric symptoms, or neurological impairment **AND** to confirm the absence of present untreated, underlying mental health conditions/issues (e.g., depression, substance abuse) as a major contributor to chronic pain

Informational Note: The behavioral algorithm for considering patients for intrathecal pain therapy includes failure of conservative therapies, psychological evaluation, medical history evaluation, and an intrathecal screening trial [PACC].

EXCEPTION: For members receiving palliative or end-of-life care where psychological and cognitive symptoms or psychiatric illnesses are commonly exacerbated or experienced. Documentation or attestation of palliative or end-of-life care required. **Recommendation:** The palliative care physician should assess for optimal psychological treatment or intervention for individuals with terminal illness which may include collaboration with psychiatrists or mental health resources.

5. Member has had a preliminary trial with a temporary intrathecal /epidural catheter to assess pain relief, degree of side effects and patient tolerability. Documentation of medication response and tolerance, including assessment in reduction of pain, increase in function and effects on the activities of daily living required for review

   Refer to 'MCP-160: Implantable Intrathecal Pain Pump' for coverage policy of a temporary trial.

6. Documentation of treatment failure at therapeutic or maximally tolerated doses for at least 3 weeks (verified via pharmacy claims if applicable), intolerance or contraindication to **ALL** the following:
   a. Non-opioid medications, including ALL the following: NSAIDs, acetaminophen, gabapentin, amitriptyline, topical lidocaine, carbamazepine, duloxetine, fluoxetine
   b. TWO short-acting and/or long-acting opioids
   c. Intrathecal morphine

7. Member does not have an infection at the injection site, uncontrolled bleeding, or spinal canal obstruction that impairs cerebrospinal fluid circulation [Contraindicated in intrathecal administration]

8. Not prescribed for, or intended for concurrent use with, **ANY** of the following:
   Treatment plan, including planned therapy modification or clinical rationale for maintaining treatment is required if member is currently on ANY of the following medications.

   a. Avoid Combination Use (may enhance the central nervous system depressant effect): azelastine (nasal), bromperidol, thalidomide, paraldehyde, orphenadrine, oxomemazine

      MOLINA MEDICAL/PHARMACY REVIEWER: Verify member's claims history, chart notes, and prescribing physician notes/attestation. Authorization is not recommended if member is on any of these medications

   b. Consider Therapy Modification: Oxycodone, buprenorphine, benzodiazepines, or other central nervous system depressants (i.e., chlormethiazole, droperidol, flunitrazepam, zolpidem, suvorexant, perampanel, opioid agonists)

      MOLINA MEDICAL/PHARMACY REVIEWER: Verify member's claims history, chart notes, and prescribing physician notes/attestation. Pharmacy/Medical Director to review treatment plan submitted and may request additional information or peer-to-peer with Prescriber if necessary

   c. Other intrathecal medication(s) *Due to the lack of safety, efficacy, and long-term drug product stability*

      MOLINA MEDICAL/PHARMACY REVIEWER: Verify the above per member's claims, chart notes, and prescribing physician notes and relevant documentation

9. Attestation of **ALL** the following:
   a. Member has been counseled and acknowledges understanding of the potential risk of psychosis or neurological impairment and wishes to proceed with treatment
   b. Prescriber will monitor member's response to treatment, including improvements to pain severity AND neurological or psychiatric signs or symptoms for duration of therapy

CONTINUATION OF THERAPY when **ALL** the following clinical criteria are met:

1. Member continues to meet initial coverage criteria appropriate for continuation of treatment
2. Documentation of continued need for intrathecal therapy and evidence of pain control
3. Member has received ongoing monitoring for neurological or psychiatric signs or symptoms throughout therapy
4. No evidence of unacceptable adverse effects or complications from ziconotide therapy, such as psychiatric symptoms and neurological impairment

LIMITATIONS AND EXCLUSIONS

1. Known allergy or hypersensitivity to ziconotide or any component of the formulation
2. Pre-existing history of psychosis
3. Other concomitant treatment(s) or medical condition(s) that would render intrathecal administration hazardous (e.g., infection at the injection site, *uncontrolled hematological disease (bleeding diathesis), spinal cord compression or any spinal canal obstruction that impairs circulation of cerebrospinal fluid)
   **Patients with clinically significant thrombocytopenia or bleeding problems such as coagulopathy, hemophilia, or von Willebrand's disease may not be appropriate candidates for ziconotide receipt.*
4. Intravenous administration
5. Concomitant treatment or medical condition that would render intrathecal administration hazardous such as the presence of infection at the micro infusion injection site, uncontrolled bleeding diathesis, and spinal canal obstruction that impairs circulation of cerebrospinal fluid
6. High risk of bleeding (e.g., history of bleeding tendency, concurrent uses of other anticoagulants/antiplatelets, liver cirrhosis or advanced liver disease, and advanced renal disease) **NOTE:** Treatment should be managed in accordance to current accepted guidelines [e.g., American Society of Interventional Pain Physicians (ASIPP 2019) Guidelines]

   EXCEPTION: Prescriber submit documentation of chart notes and treatment plan for review, if applicable.

7. Requested dose and frequency is not in accordance with FDA-approved labeling, nationally recognized compendia, and/or evidence-based practice guidelines. **NOTE:** Doses above 19.2 µg/day (0.8 µg/hr.) will not be authorized

The following are considered **experimental, investigational, and unproven** based on insufficient evidence:

1. Any indication other than those listed above
   Based on the peer-reviewed medical literature the safety and effectiveness for indications other than the medically necessary indication listed above has not been established.

DURATION OF APPROVAL AND QUANTITY LIMITATIONS

1. Dose does not exceed 19.2 mcg/day (0.8 mcg/hour)
2. Initial Therapy: May authorize up to 3 months of initial therapy
3. Continuation of therapy: May be authorized up to 6 months. Subsequent approval will be based on continuous progress notes from the Prescriber documenting improvement from baseline.

ADMINISTRATION

1. Not for intravenous administration or epidural administration. For intrathecal administration only using Medtronic SynchroMed II Infusion System, or CADD-Micro ambulatory infusion pump.
2. Refer to Specialty Medication Administration Site of Care Policy P&P: MHI Pharm 11.
3. If member meets all criteria and approval for therapy is granted, medication will be dispensed by a specialty pharmacy vendor at the discretion of Molina Healthcare.

DOSING CONSIDERATIONS

Chronic pain (intolerant or refractory to other therapies)

- Initial dose: ≤ 2.4 mcg/day (≤ 0.1 mcg/hour). Initiating with more conservative dosing is preferred due to improved tolerability

  Alternate initial dosing (Off-label): 0.5 to 1.2 mcg/day (0.02 to 0.05 mcg/hour) (McDowell, Pope 2016). Initiating with no more than 0.5 mcg/day (0.02 mcg/hour) may be preferred (Prager, 2014).

- Dosage titration: According to the manufacturer, dose may be titrated by ≤ 2.4 mcg/day (≤ 0.1 mcg/hour) at intervals ≤ 2 to 3 times/week to a maximum dose of 19.2 mcg/day (0.8 mcg/hour) by day 21; average dose at day 21: 6.9 mcg/day (0.29 mcg/hour). However, expert consensus recommends upward titration (based

on analgesia and tolerability) in increments of no more than 0.5 mcg/day (≤0.02 mcg/hour) and not more often than once weekly (McDowell 2016; Prager 2014). A faster titration should be used only if the urgent need for analgesia outweighs the possible risk to patient safety.

MONITORING PARAMETERS: Psychiatric or neurological impairment; signs and symptoms of meningitis or other infection; serum creatine phosphokinase (every other week for first month then monthly); pain relief.

DOCUMENTATION REQUIREMENTS. Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DRUG INFORMATION

ROUTE OF ADMINISTRATION: For intrathecal administration only using programmable implanted variable-rate micro infusion device (Medtronic SynchroMed EL or SynchroMed II) or external micro infusion device and catheter (CADD-Micro ambulatory infusion pump)

DRUG CLASS: Analgesic, Nonopioid; Calcium Channel Blocker, N-Type

FDA-APPROVED USES: Chronic pain
Management of severe chronic pain in patients for whom intrathecal therapy is warranted and who are intolerant of, or refractory to, other treatment (e.g., systemic analgesics, adjunctive therapies, intrathecal morphine). December 28, 2004. Updated Labeling-Package Insert dated March 2023 re-affirms indications and usage.

NOTE: Dosage should be titrated according to the pain severity, patient response, and adverse event occurrence. Reduced initial dosages should be considered for elderly patients and for patients receiving central nervous system depressants.

RISK EVALUATION AND MITIGATION STRATEGY (REMS): N/A

BOXED WARNING: Severe psychiatric symptoms and neurological impairment may occur during treatment with ziconotide. Do not treat patients with a preexisting history of psychosis with ziconotide. Monitor all patients frequently for evidence of cognitive impairment, hallucinations, or changes in mood or consciousness. Discontinue ziconotide in the event of serious neurologic or psychiatric signs or symptoms. Ziconotide therapy can be interrupted or discontinued abruptly without evidence of withdrawal effects.

SUMMARY OF MEDICAL EVIDENCE

Randomized Controlled Trials
Rauck et al. (2006) conducted a double-blind, placebo-controlled study in 220 patients with chronic, noncancer refractory to conventional treatment to reduce side effects and increase tolerability. A total of 220 patients with severe chronic pain were randomly assigned to one of two groups: ziconotide (n=112) or placebo (n=108). The initial dose of ziconotide was 2.4 mcg/day (0.1 mcg/hr), and it could be increased by 2.4 mcg/day (0.1 mcg/hr) two to three times per week (minimum titration interval 24 hours) to a maximum dose of 19.2 mcg/day (0.8 mcg/hr). At the end of the trial after 21 days, the final mean dose was 6.9 mcg/day (0.29 mcg/hr). At the outset, 97% of these patients reported that their pain was refractory to treatment, which included intrathecal morphine, intrathecal bupivacaine (an off-label use for this drug), and/or intrathecal clonidine (an off-label use for this drug) in addition to systemic analgesics and adjunctive therapy. All intrathecal medications were stopped for one to three weeks, and patients were kept on a stable regimen of non- intrathecal analgesics, including opiates, for at least seven days before randomization. This period was completed successfully by 93% of the patients who were screened. The ziconotide group experienced dizziness, confusion, ataxia, abnormal gait, and memory impairment. Both groups had comparable rates of discontinuation for adverse events and serious adverse events. Slow titration of ziconotide, a nonopioid analgesic, to a low maximum dose resulted in significantly better pain relief and tolerance than two previous controlled trials that used a faster titration to a higher mean dose. The Mini Mental State Examination results revealed no significant

changes in mental status and no differences between the ziconotide and placebo groups. During this study, however, no cases of respiratory depression, drug dependence, or withdrawal symptoms (potential risks of opioid administration) were reported, and there was no evidence of tolerance to ziconotide or granuloma formation at the tip of the intrathecal catheter (as is observed rarely during intrathecal opioid treatment in association with neurological sequelae). Overall, the findings indicate that intrathecal ziconotide infusion therapy may be an option for patients suffering from severe, refractory chronic pain. Because there was no comparator group in the study, the efficacy data should be interpreted with caution. A significant limitation of this study is that rare adverse events are unlikely to have been detected.

Wallace et al. (2006) evaluated ziconotide in a double-blind placebo-controlled study involving 257 patients with refractory, intractable nonmalignant pain. Intrathecal ziconotide (n=170) or placebo (n=87) was administered to the patients. Pain was classified as neuropathic or nociceptive with a chronic nonmalignant etiology. The mean percent Visual Analogue Scale of Pain Intensity (VASPI) improvement for ziconotide was 31.2% versus 6.0% for placebo (p ≤ 0.001), with 33.7% of ziconotide patients reported as responders versus 12.8% for placebo (p 0.001). Finally, 43.8% of ziconotide patients reported moderate or better pain relief, with 8.9% reporting complete pain relief, compared to only 17.4% of placebo patients reporting moderate or greater pain relief, with no patients reporting complete pain relief. The first 28% of patients enrolled received an initial infusion rate of 0.4 mcg/h, with the dosage titrated to a maximum of 7 mcg/h; however, poor tolerability prompted a change in the dosing regimen. In 72% of patients, therapy was started at 0.1 mcg/h and gradually increased to 2.4 mcg/h over 5 to 6 days. The baseline VASPI score in the ziconotide group was 80.2 mm and 76.8 mm in the placebo group. The mean VASPI improvement with the lower-dosage regimen was 31.8% in the ziconotide group and 6.6% in the placebo group (P = 0.002). Most adverse events were nervous system-related, such as dizziness, confusion, urinary retention, nausea, vomiting, and amblyopia.

Staats et al. (2004) conducted a multi-center, double-blind, placebo-controlled, randomized study in 111 patients (n = 111) with cancer or AIDS to assess the safety and efficacy of ziconotide in patients with pain that is refractory to conventional treatment. Patients ranged in age from 24 to 85 years old, had cancer or AIDS, and had a mean VASPI score of 50mm or higher despite treatment with a systemic or intrathecal analgesic regimen. Subjects were randomly assigned to either ziconotide or placebo treatment in a 2:1 ratio. Patients were randomly assigned to either ziconotide (n=71) or a placebo (n=40). Intrathecal ziconotide was titrated over 5 to 6 days for responders, followed by a 5-day maintenance phase. Those who did not respond were switched to the alternate treatment. At the start of the study, 67 of 68 (98.5%) evaluable patients in the ziconotide group and 38 of 40 (95%) in the placebo group were on opioids (median morphine equivalent dosage of 300 mg/day in the ziconotide group and 600 mg/day in the placebo group). At baseline, the ziconotide group had a mean VASPI of 73.6 mm and the placebo group had a mean VASPI of 77.9 mm. The ziconotide group improved 53.1% (95% CI, 44% to 62.2%), while the placebo group improved 18.1% (95% CI, 4.8% to 31.4%) (P 0.001). During the maintenance phase, the ziconotide group's efficacy did not decline. Pain relief was moderate to complete in 52.9% of ziconotide-treated patients compared to 17.5% of placebo patients (P < 0.001). Five patients in the ziconotide group were completely pain-free. Opioid use declined by 9.9% in the ziconotide group but rose by 5.1% in the placebo group. At the end of the crossover phase, 26 patients in the placebo group switched to ziconotide therapy and experienced a 44.9% mean reduction in VASPI score. The study concluded that intrathecal ziconotide provided clinically and statistically significant analgesia in patients with pain from cancer or AIDS.

Atanasoff et al. (2000) assessed intrathecal ziconotide in a double-blind pilot study involving 30 patients undergoing elective total abdominal hysterectomy, radical retropubic prostatectomy, or total hip replacement. A continuous intrathecal infusion of either placebo or ziconotide 0.7 mcg/h or 7 mcg/h was started after a local anesthetic injection in the intrathecal and continued for 48 to 72 hours post-operatively. Efficacy was assessed in 26 patients. Seventeen patients [9 of 12 (75%) in the placebo group, 5 of 12 (42%) in the low-dose group, and 3 of 6 (50%) in the high-dose group] requested additional narcotics or ketorolac. Patients in the high-dose group received 6.6 mg of morphine equivalent between 24 and 48 hours after surgery, compared to 20.7 mg of morphine equivalent in the low-dose group. The ziconotide-treated patients had significantly lower VASPI scores during the first 8 postoperative hours. Ziconotide-treated patients had decreased VASPI ratings after 8 hours. High dose ziconotide patients experienced more side events that required therapy discontinuation. It was noted that the high dose was accompanied with undesirable side effects, and the low dose was only marginally more beneficial than placebo, therefore the optimal amount for postoperative pain may fall somewhere in between and closer to the lower dose.

Non-Randomized Studies, Retrospective Reviews, and Other Evidence

Brinzeu et al. (2019) conducted a cohort study on patients with central neuropathic pain related to spinal cord injury refractory to medical pain management. Patients willing to participate were tested by lumbar puncture injection of ziconotide or continuous intrathecal infusion and if a significant decrease in pain scores (>40%) was noted they were implanted with a continuous infusion pump. In total, twenty participants were enrolled in the study. Of the twenty, 14 had decreased pain scores of more than 40% but only 11 (55%) were implanted with permanent pumps due to side effects and patient choice. These were followed up on average for 3.59 years (±1.94) and in eight patients a decrease in pain scores was maintained. Overall, in patients that responded to the test baseline VASPI was 7.91 and 4.31 at last follow-up with an average dose of 7.2 µg of ziconotide per day. Six patients (30%) did not respond to any test and in three patients side effects precluded pump implantation. No significant long-term effects were noted.

Deer et al. (2018) conducted an interim analysis of the open label long term multicenter observational study data collection of the Patient Registry of Intrathecal Ziconotide Management (PRIZM). The interim analysis, data through July 2015, compared ziconotide as the first vs. not first intrathecal agent in pump and used the Numeric Pain Rating Scale and Patient Global Impression of Change scores as measurements from baseline. Ninety-three patients were included in the analysis with results as follows: Fifty-one patients (54.8%) received ziconotide as the first agent in pump (FIP+), whereas 42 (45.2%) did not (FIP-). Mean baseline Numeric Pain Rating Scale scores were 7.4 (1.9) and 7.9 (1.6) in FIP+ and FIP- patients, respectively. Mean percentage changes in Numeric Pain Rating Scale scores were -29.4% (5.5%) in FIP+ patients (n = 26) and +6.4% (7.7%) in FIP- patients (n = 17) at month 6 and -34.4% (9.1%) in FIP+ patients (n = 14) and -3.4% (10.2%) in FIP- patients (n = 9) at month 12. Improvement from baseline, measured by Patient Global Impression of Change score, was reported in 69.2% of FIP+ (n = 26) and 35.7% of FIP- (n = 14) patients at month 6 and 85.7% of FIP+ (n = 7) and 71.4% of FIP- (n = 7) patients at month 12. The most common adverse events (≥ 10% of patients overall as of the data cut) were nausea (19.6% vs. 7.1% of FIP+ vs. FIP- patients, respectively), confused state (9.8% vs. 11.9%), and dizziness (13.7% vs. 7.1%).

National and Specialty Organizations

The **American Society of Regional Anesthesia and Pain Medicine and American Society of Anesthesiologists (ASRA-ASA)** issued practice guidelines for chronic pain management in 2010 to update a previous version from 1997. According to the guidelines, observational studies show that intrathecal opioid injections can provide effective pain relief for 1 to 12 months in patients with neuropathic pain. Intrathecal opioid administration is recommended for patients with neuropathic pain. However, a discussion of potential complications should be included in shared decision making regarding this procedure. Additionally, a neuraxial opioid trial should be performed before intrathecal drug delivery systems are permanently implanted (ASRA-ASA, 2010).

The **Polyanalgesic Consensus Conference (PACC)** panel developed an intrathecal drug selection algorithm. Since then, the review and algorithm have been updated three times, most recently in 2017 and 2018 ([1-2]Deer et al. 2017).

The 2016 consensus conference did not distinguish between nociceptive and neuropathic pain because many chronic pain syndrome patients have both forms of pain. Instead, it provided separate guidance for localized and diffuse pain.

- Both morphine and ziconotide were recommended as first-line intrathecal monotherapy for localized and diffuse chronic pain of cancer-related and non-cancer-related etiologies in the 2016 guidelines; however, one consensus point emphasized ziconotide use as first-line intrathecal therapy in patients with chronic non-cancer-related pain, unless contraindicated.
- Failure of conservative therapies, psychological evaluation, medical history evaluation, and an intrathecal screening trial comprise the behavioral algorithm for considering patients for intrathecal pain therapy.
- Morphine, ziconotide, or morphine + bupivacaine is recommended first-line treatments for neuropathic pain if patients undergo intrathecal drug delivery system implantation.
- First-line treatments for nociceptive pain include morphine, hydromorphone, ziconotide, and fentanyl.
- The recommended starting dose for ziconotide is 0.5 to 2.4 micrograms per day.
- There was also evidence of an increased risk of death immediately after reinitiating intrathecal opioids or performing a revision to the drug delivery system. Patients with sleep apnea, psychiatric conditions, or who are taking certain medications or supplements should be monitored more frequently and vigilantly.

The 2017 update primarily addresses the controversial topic of intrathecal trialing. The recommendations for trialing are presented in 34 consensus points and cover trialing for morphine, ziconotide, and medication admixtures. The recommendations address starting doses, titration practices, measurements of success, trial settings and monitoring, management of systemic oral opioids during trialing, and the role of psychological evaluation. The recommendations also describe clinical scenarios in which IT trialing is required or not required ([3]Deer et al. 2017).

In 2024 **PACC** (Deer et al.) published guidance on intrathecal drug delivery for chronic noncancer pain. The 2024 **PACC** update provides best practices on intrathecal drug delivery to improve safety and efficacy. The information is presented in 32 consensus points, with content on ziconotide intrathecal trialing, starting dose, titrating dosing, side effects and need for a creatinine kinase level at baseline and with onset of new muscle pain and/or weakness.

- "Intrathecal trialing of ziconotide may be best performed using injections of small boluses as opposed to continuous infusion,
- The starting dose for intrathecal ziconotide infusion should be 0.5 to 1.0 micrograms per day.
- When titrating intrathecal ziconotide dosing, an increase of no more than 0.5 micrograms per day with weekly reassessment is warranted.
- When side effects occur, it is recommended to reduce the intrathecal infusion dose of the ziconotide to the last tolerated level that relived pain without side effects.
- A baseline creatinine kinase level should be obtained before intrathecal infusion is initiated and whenever symptoms of muscle weakness or pain manifest with long-term infusion."

SUPPLEMENTAL INFORMATION

Visual Analogue Scale of Pain Intensity (VASPI): A globally validated, subjective measure for acute and chronic pain. A VAS score for pain is calculated by drawing a horizontal line 100 millimeters (mm) long and anchoring it with word descriptors at each end; "no pain" (0 mm) on the left end and "worst imaginable pain" (100 mm) on the right. The participant indicates on the line the point that, in their opinion, best represents their current level of pain.

CODING & BILLING INFORMATION

HCPCS (Healthcare Common Procedure Coding System)

Code	Description
J2278	Injection, ziconotide, 1 mcg

AVAILABLE DOSAGE FORMS: Solution, intrathecal, as acetate [preservative free]: Prialt: 500 mcg/20 mL (20 mL); 100 mcg/mL (1 mL); 500 mcg/5 mL (5 mL)

CODING DISCLAIMER. Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY

10/09/2024	Policy reviewed**,** no changes to coverage criteria, updated Summary of Medical Evidence and References. IRO Peer Review on September 3, 2024 by a practicing physician board-certified in Physical Medicine and Rehabilitation; Pain Medicine.
12/13/2023	Policy reviewed, no changes to coverage criteria, updated references.
12/14/2022	Policy reviewed, no changes to coverage criteria, updated references.
12/08/2021	Policy reviewed, no changes to coverage criteria, updated references; added relevant professional society guidelines.
12/09/2020	New policy. IRO Peer Review: 10/9/2020. Practicing physician board certified in Physical Med & Rehab, Pain Management.

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