PRIOR AUTHORIZATION POLICY

POLICY: Opioids – Tramadol Extended-Release Products Prior Authorization Policy
- ConZip® (tramadol hydrochloride extended-release capsules – Vertical)
- Tramadol extended-release capsules – various (brand products)
- Tramadol hydrochloride extended-release tablets – generic to the discontinued product Ultram® ER
- Tramadol hydrochloride extended-release tablets – generic to the discontinued product Ryzolt™

REVIEW DATE: 01/24/2024

OVERVIEW

Tramadol extended-release tablets, tramadol extended-release capsules, and ConZip are indicated for the **management of severe and persistent pain that requires an extended treatment period with a daily opioid analgesic** and for which alternative treatment options are inadequate.[1-3]

Tramadol is a centrally acting synthetic opioid analgesic.[1-3] The extended-release tramadol products differ in their extended-release mechanism. ConZip contains a total dose of tramadol in a combination of immediate-release and extended-release components. However, ConZip is bioequivalent to a reference extended-release tramadol product under fasting conditions. Therefore, clinical efficacy was based on a reference extended-release tramadol product.

Guidelines

In 2022, the **Centers for Disease Control and Prevention (CDC)** published an updated guideline for prescribing opioids for pain.[4] Nonopioid therapies are at least as effective as opioids for many common types of acute pain, and nonopioid therapies are preferred for subacute and chronic pain. Clinicians should maximize the use of nonpharmacologic and nonopioid pharmacologic therapies as appropriate for the specific condition and patient and only consider initiating opioid therapy if expected benefits for pain and function are anticipated to outweigh risks to the patient. Multiple noninvasive nonpharmacologic interventions (e.g., aerobic, aquatic, or resistance exercises, weight loss, psychological therapy, spinal manipulation, low-level laser therapy, massage, mindfulness-based stress reduction, yoga, tai chi, qigong, acupuncture, cognitive behavioral therapy, and spinal manipulation) are associated with improvements in pain, function, or both, that are sustained after treatment and are not associated with serious harms. Non-opioid drugs (e.g., tricyclic antidepressants, serotonin and norepinephrine reuptake inhibitor [SNRI] antidepressants, duloxetine, selected antiseizure medications (e.g., pregabalin, gabapentin, oxcarbazepine), capsaicin and lidocaine patches, and nonsteroidal anti-inflammatory drugs [NSAIDs]) are associated with small to moderate improvements in chronic pain and function for certain chronic pain conditions.

Before initiating opioid therapy for patients with pain, clinicians should discuss with patients the realistic benefits and known risks of opioid therapy.[4] Before starting ongoing opioid therapy for patients with subacute or chronic pain, clinicians should work with patients to establish treatment goals for pain and function and consider how opioid therapy will be discontinued if benefits do not outweigh risks. When opioids are initiated, clinicians should prescribe the lowest effective dosage of immediate-release opioids for no longer than needed for the expected duration of pain severe enough to require opioids. During ongoing opioid therapy, clinicians should collaborate with patients to evaluate and carefully weigh the benefits and risks of continuing opioid therapy and exercise care when increasing, continuing, or reducing opioid dosage. The guideline recommends that clinicians should not initiate opioid treatment with long-acting (LA) opioids for patients who are opioid-naïve and should not prescribe LA opioids for intermittent

use. LA opioids should be reserved for severe, continuous pain. Before starting and periodically during continuation of opioid therapy, clinicians should evaluate the risk for opioid-related harms and should work with patients to incorporate relevant strategies to mitigate risk, including offering naloxone and reviewing potential interactions with any other prescribed medications or substances used. When prescribing initial opioid therapy and periodically during opioid therapy, clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or combinations that put the patient at high risk for overdose. When prescribing opioids for subacute or chronic pain, clinicians should consider the benefits and risks of toxicology testing to assess for prescribed medications as well as other prescribed and nonprescribed controlled substances.

The 2020 **American Society of Hematology** guideline for the management of acute and chronic pain in patients with sickle cell disease states that pain causes significant morbidity for those living with sickle cell disease and manifests as acute intermittent pain, chronic daily pain, and acute-on-chronic pain.[5] For adults and children with chronic pain who are receiving chronic opioid therapy, are functioning well, and have perceived benefit, the guideline suggests shared decision making for continuation of chronic opioid therapy. For adults and children with chronic pain who are receiving chronic opioid therapy, are functioning poorly, or are at high risk for aberrant opioid use or toxicity, the guideline suggests against continuation of chronic opioid therapy.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of tramadol extended-release products. Tramadol extended-release products are controlled substances (CIV) which can be misused and abused. Because of the specialized skills required for evaluation and diagnosis of patients with sickle cell disease as well as the monitoring required for adverse events and long-term efficacy, approval requires tramadol extended-release products to be prescribed by or in consultation with a hematologist for patients with this diagnosis. All approvals are provided for the duration noted below.

Automation: A patient with a history of a tramadol extended-release product within the 130-day look-back period is excluded from Prior Authorization. If a patient has a prescription for a cancer medication (see Appendix A) within a 180-day period, the claim will adjudicate. When available, the ICD-10 codes for cancer will be used as part of automation to allow approval of the requested medication (see Appendix B).

RECOMMENDED CRITERIA

Coverage of a tramadol extended-release product is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Pain Severe Enough to Require Daily, Around-the-Clock, Long-Term Opioid Treatment.** Approve for 1 year if the patient meets ONE of the following (A, B, C, or D):
   - **A)** Patient has a cancer diagnosis; OR
   - **B)** Patient is in hospice program, end-of-life care, or palliative care; OR
   - **C)** Patient meets BOTH of the following criteria (i and ii):
     - **i.** Patient has diagnosis of sickle cell disease; AND
     - **ii.** Medication is prescribed by or in consultation with a hematologist; OR
   - **D)** Patient meets all of the following (i, ii, iii, iv, v, vi, and vii):
     - **i.** Patient is not opioid-naïve; AND

ii. Non-opioid therapies have been optimized and are being used in conjunction with opioid therapy according to the prescriber; AND
Note: Examples of non-opioid therapies include non-opioid medications (e.g., nonsteroidal anti-inflammatory drugs, tricyclic antidepressants, serotonin and norepinephrine reuptake inhibitors, antiseizure medications), physical therapy, exercise therapy, weight loss, and cognitive behavioral therapy.

iii. Patient's of controlled substance prescriptions has been checked using the state prescription drug monitoring program (PDMP), according to the prescriber; AND

iv. Risks (e.g., addiction, overdose) and realistic benefits of opioid therapy have been discussed with the patient, according to the prescriber; AND

v. Treatment plan (including goals for pain and function) is in place and reassessments (including pain levels and function) are scheduled at regular intervals, according to the prescriber; AND

vi. Need for a naloxone prescription has been assessed and naloxone has been ordered, if necessary, according to the prescriber; AND

vii. Need for periodic toxicology testing has been assessed and ordered, if necessary, according to the prescriber.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of a tramadol extended-release product is not recommended in the following situations:

1. **Acute Pain.** According to the CDC guideline for prescribing opioids for chronic pain, clinicians should not prescribe extended-release/long-acting opioids for the treatment of acute pain due to the longer half-lives and longer duration of effects (e.g., respiratory depression) with extended-release/long-acting opioids.[4]

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Tramadol hydrochloride extended-release tablets [prescribing information]. Baltimore, MD: Lupin; January 2024.
2. ConZip® [prescribing information]. Bridgewater, NJ: Vertical; December 2023.
3. Tramadol Hydrochloride Extended-Release Capsules [prescribing information]. Alpharetta, GA: Trigen; January 2022.
4. Dowell D, Ragan KR, Jones CM, et al. CDC Clinical Practice Guideline for Prescribing Opioids for Pain - United States, 2022. *MMWR Recomm Rep*. 2022;71(3):1-95.
5. Brandow AM, Carroll CP, Creary S, et al. American Society of Hematology 2020 guidelines for sickle cell disease: management of acute and chronic pain. *Blood Adv*. 2020;4(12):2656-2701.

APPENDIX A

Note: This list is not inclusive. As new STCs become available, they will roll into this policy and the list will be updated periodically.

* Excluding topical products.

APPENDIX B

*Indicates the inclusion of subheadings.