PRIOR AUTHORIZATION POLICY

POLICY: Opioids – Tramadol Extended-Release Prior Authorization Policy

- ConZip® (tramadol hydrochloride extended-release capsules – Vertical)
- Tramadol extended-release capsules – various (brand products)
- Tramadol hydrochloride extended-release tablets – generics to the discontinued product Ultram® ER
- Tramadol hydrochloride extended-release tablets – generics to the discontinued product Ryzolt

REVIEW DATE: 08/19/2020

OVERVIEW

Tramadol extended-release tablets, tramadol extended-release capsules, and ConZip are indicated for the management of pain severe enough to require daily around-the-clock, long-term opioid treatment 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 2016, the Centers for Disease Control (CDC) published a guideline for prescribing opioids for chronic pain.[4,5] The guideline provides recommendations for primary care providers who are prescribing opioids for chronic pain outside of active cancer treatment, palliative care, and end-of-life care. In the guideline, chronic pain is defined as pain that typically lasts greater than 3 months or past the time of normal tissue healing, resulting from an underlying medical disease or condition, injury, medical treatment, inflammation, or an unknown cause. To support the guideline an updated review of long-term opioid therapy for chronic pain outside of end-of-life care was undertaken and the results revealed that evidence remains limited, with insufficient evidence to determine long-term benefits of chronic opioid therapy versus no opioid therapy. However, the evidence did suggest a risk for serious harms with long-term opioid therapy that appears to be dose-dependent.

The CDC guidelines recommend non-pharmacologic therapy and non-opioid pharmacologic therapy for chronic pain; if opioids are used, they should be combined with non-pharmacologic therapy and non-opioid pharmacologic therapy, as appropriate.[4] Before starting and periodically during opioid therapy, healthcare providers should discuss with their patient the risks and realistic benefits of opioid therapy and also the shared responsibilities for managing therapy. When starting opioid therapy for chronic pain, immediate-release opioids should be prescribed at the lowest effective dosage instead of initiating therapy with extended-release/long-acting opioids. Before starting and periodically during continuation of opioid therapy, healthcare providers should evaluate risk factors for opioid-related harms and incorporate strategies into the management plan to mitigate risk, including offering naloxone. The patient's history of controlled substance prescriptions should be periodically reviewed using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations putting them at high risk for overdose. Urine drug testing is recommended before starting opioid therapy and at least annually to assess for prescribed medications as well as other controlled

prescription drugs and illicit drugs; treatment should be offered to and/or arranged for patients with opioid use disorder.

The CDC guideline states that long-term opioid use often begins with treatment of acute pain.[4] When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids, i.e., ≤ 3 days and only rarely > 7 days.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of tramadol extended-release products. Tramadol extended-release products are controlled substances (C-IV) which can be misused and abused. Additionally, due to the availability of generic tramadol extended-release tablets, approval of a branded tramadol extended-release product requires a previous trial of the generic. All approvals are provided for the duration noted below.

Automation: If a generic tramadol extended-release product is requested and the patient has history of a generic tramadol extended-release product within the 130-day look-back period, a prescription for a cancer medication (see Appendix A) within a 180-day period, or an ICD-10 code for cancer (see Appendix B), the claim will adjudicate.

RECOMMENDED CRITERIA

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

FDA-Approved Indications

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 criteria (A, B or C) AND D:
   - **A)** Patient has a cancer diagnosis; OR
   - **B)** Patient is in hospice program, end-of-life care, or palliative care; OR
   - **C)** Patient has chronic pain but does not have a cancer diagnosis. Approve for 1 year if the patient meets ALL of the following criteria (i, ii, iii, iv, and v):
     - **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, anticonvulsants), exercise therapy, weight loss, and cognitive behavioral therapy.
     - **iii.** Patient's history of controlled substance prescriptions has been checked using the state prescription drug monitoring program (PDMP), unless unavailable in the state (see note below), according to the prescriber; AND
       Note: As of 08/19/2020, the state of Missouri is the only state in the US that does not have a statewide PDMP program in place.
     - **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.

D) If a branded tramadol extended-release product is requested, the patient has tried generic tramadol extended-release tablets.

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. Ultram® ER [prescribing information]. Titusville, NJ: Janssen Pharmaceuticals Inc.; August 2017.
2. Conzip® [prescribing information]. Bridgewater, NJ: Vertical Pharmaceuticals, Inc.; October 2019.
3. Tramadol Hydrochloride Extended-Release Capsules [prescribing information]. Bridgewater, NJ: Trigen Laboratories, LLC; October 2019.
4. Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. MMWR Recommendations and Reports. 2016;65(1):1-49.
5. Centers for Disease Control and Prevention. Checklist for prescribing opioids for chronic pain. Available at: https://www.cdc.gov/drugoverdose/pdf/pdo_checklist-a.pdf. Accessed on August 17, 2020.

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.

STC*	STC Description
0470	ANTINEOPLASTIC - ALKYLATING AGENTS
0471	ANTINEOPLASTIC - ANTIMETABOLITES
0472	ANTINEOPLASTIC - VINCA ALKALOIDS
0473	ANTIBIOTIC ANTINEOPLASTICS
0475	ANTINEOPLASTICS, MISCELLANEOUS
6323	ANTINEOPLASTIC - ANTIANDROGENIC AGENTS
7235	ANTINEOPLASTICS ANTIBODY/ANTIBODY-DRUG COMPLEXES
7977	ANTINEOPLASTIC IMMUNOMODULATOR AGENTS
8254	ANTINEOPLASTIC LHRH(GNRH) AGONIST, PITUITARY SUPPR.
8460	ANTINEOPLASTIC LHRH(GNRH) ANTAGONIST,PITUIT.SUPPRS
8569	ANTINEOPLASTIC EGF RECEPTOR BLOCKER MCLON ANTIBODY
8585	ANTINEOPLAST HUM VEGF INHIBITOR RECOMB MC ANTIBODY
9150	ANTINEOPLASTIC SYSTEMIC ENZYME INHIBITORS
B759	ANTINEOPLAST, HISTONE DEACETYLASE (HDAC) INHIBITORS
C232	ANTINEOPLASTIC - MTOR KINASE INHIBITORS
C370	ANTINEOPLASTIC - EPOTHILONES AND ANALOGS
C532	ANTINEOPLASTIC - TOPOISOMERASE I INHIBITORS
C593	ANTINEOPLASTIC - AROMATASE INHIBITORS
D426	ANTINEOPLASTIC - IMMUNOTHERAPY, THERAPEUTIC VAC
D560	ANTINEOPLASTIC - HALICHONDRIN B ANALOGS
D687	CYTOTOXIC T-LYMPHOCYTE ANTIGEN (CTLA-4) RMC ANTIBODY

E039	ANTINEOPLASTIC - JANUS KINASE (JAK) INHIBITORS
E150	ANTINEOPLASTIC - HEDGEHOG PATHWAY INHIBITOR
E600	ANTINEOPLASTIC - VEGF-A,B AND PLGF INHIBITORS
F495	ANTINEOPLASTIC - INTERLEUKIN-6(IL-6)INHIB,ANTIBODY
F501	ANTINEOPLASTIC - VEGFR ANTAGONIST
F665	ANTINEOPLASTIC, ANTI-PROGRAMMED DEATH-1 (PD-1) MAB
G545	ANTINEOPLASTIC - IMMUNOTHERAPY, VIRUS-BASED AGENTS
G575	ANTINEOPLASTIC - MEK1 AND MEK2 KINASE INHIBITORS
G590	ANTINEOPLASTIC - ANTI-CD38 MONOCLONAL ANTIBODY
G607	ANTINEOPLASTIC - ANTI-SLAMF7 MONOCLONAL ANTIBODY
G802	ANTINEOPLASTIC- B CELL LYMPHOMA-2(BCL-2) INHIBITORS
G857	ANTI-PROGRAMMED CELL DEATH-LIGAND 1 (PD-L1) MAB
H018	ANTINEOPLASTIC, PDGFR-ALPHA BLOCKER MC ANTIBODY
H214	ANTINEOPLASTIC COMB-KINASE AND AROMATASE INHIBIT
H289	ANTINEOPLASTIC-ISOCITRATE DEHYDROGENASE INHIBITORS
H309	ANTINEOPLASTIC – ANTIBIOTIC AND ANTIMETABOLITE
H317	ANTINEOPLASTIC – CD22 ANTIBODY-CYTOTOXIC ANTIBIOTIC
H324	ANTINEOPLASTIC- CD19 DIR. CAR-T CELL IMMUNOTHERAPY
H329	ANTINEOPLASTIC – CD33 ANTIBODY-CYTOTOXIC ANTIBIOTIC
H617	ANTINEOPLASTIC – BRAF KINASE INHIBITORS
H768	ANTINEOPLASTIC-CD22 DIRECT ANTIBODY/CYTOTOXIN CONJ
H868	ANTINEOPLASTIC-CD123-DIRECTED CYTOTOXIN CONJUGATE
I054	ANTINEOPLASTIC-SELECT INHIB OF NUCLEAR EXP (SINE)
I264	ANTINEOPLASTIC – PROTEIN METHYLTRANSFERASE INHIBITORS

* Excluding topical products

APPENDIX B

ICD-10 Codes
Cancer-related codes
C00.* to D09.*
D3A.* to D48.*
E34.0*
Q85.0*

*Indicates the inclusion of subheadings.