Tramadol Acetaminophen

Description

Ultram (tramadol), Ultram ER (tramadol extended-release tablets); Conzip (tramadol extended-release capsules), Ultracet (tramadol / acetaminophen)

Background
Tramadol is a centrally acting synthetic opioid analgesic used to treat moderate to moderately severe chronic pain in adults. Along from analgesia, tramadol may produce symptoms including dizziness, somnolence, nausea, constipation, sweating and pruritis similar to opioids. Tramadol has been shown to inhibit reuptake of norepinephrine and serotonin, as have some other opioid analgesics. Like with other opioids, all patients require monitoring for signs of abuse and addiction, because use of opioid analgesic products carries the risk of addiction (1).

Regulatory Status
FDA-approved indications: Ultram (tramadol) is indicated for the management of moderate to moderately severe pain in adults (1). Ultram ER and Conzip are opioid agonists indicated for the management of moderate to moderately severe chronic pain in adults who require around-the-clock treatment of their pain for an extended period of time (2-3). Ultracet is indicated for the short-term (five days or less) management of acute pain (4).

The development of a potentially life-threatening serotonin syndrome may occur with the use of tramadol products, including Ultram and Conzip, particularly with concomitant use of serotonergic drugs such as SSRIs, SNRIs, TCAs, MAOIs, and SRAs (triptans);with drugs which impair metabolism of serotonin (including MAOIs); and with drugs which impair metabolism of tramadol (CYP2D6 and CYP3A4 inhibitors). This may occur with the recommended dose (1-3).
Possible illegal or illicit use should be considered when prescribing or dispensing Ultram in situations where the physician or pharmacist is concerned about an increased risk of misuse, abuse, or diversion. Misuse or abuse poses a significant risk to the patient that could result in overdose and death. Tramadol should be used in caution with patients with respiratory depression, head trauma, and when used in conjunction with alcohol or other drugs that cause central nervous system depression (1,3).

Ultram has a maximum dose of 400mg per day due to increased risk of adverse side effects. Ultracet, Ultram ER and Conzip have a maximum daily dose 300mg. Acute overdose may induce miosis, respiratory depression, seizures, hypotonicity, and acidosis. Chronic side effects include fatigue, dizziness, vertigo, headache, visual disorders, nausea, vomiting, sweating, dry mouth, constipation, premature heartbeats, euphoria, dysphoria, and hallucinations Seizures have been reported in patients receiving tramadol. Studies have shown Tramadol-induced seizure is dose dependent (5). Ultracet, a combination of tramadol and acetaminophen, has a boxed warning regarding acetaminophen use in excess of 4,000 mg per day. Acetaminophen has been associated with acute liver failure, at times resulting in liver transplant and death. Ultram should not be used concomitantly with other acetaminophen-containing products (4).

The safety and efficacy of Ultram ER and Conzip in patients under 18 years of age have not been established (2,3).

The safety and efficacy of Ultram and Ultracet in patients under 16 years of age have not been established (1).

Related policies
Duragesic, Hysingla ER, Morphine Drug Class, Nucynta, Oxycodone, Xartemis XR, Zohydro ER

Policy
This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Ultram and Ultracet may be considered medically necessary in patients that are 16 years of age and older with moderate to severe pain. Ultram ER and Conzip may be considered medically necessary in patient that are 18 years of age and older requiring management of moderate to severe chronic pain in adults who require around-the-clock treatment of their pain for an extended period of time.
Ultram may be considered investigational in patients that are under the age of 16 and do not have moderate to severe pain. Ultram ER; Conzip may be considered investigational in patients that are under the age of 18 and do not have moderate to severe chronic pain requiring around-the-clock treatment.

Prior-Approval Requirements

Diagnosis

**Ultram (tramadol)**

**Age**

16 years of age or older

Patient must have the following:

Moderate to severe pain

**AND** the following:

1. Physician agrees to taper patient’s dose to the maximum FDA allowable dose based on their daily dose
   a. Patients taking over 600mg daily will be required to taper to 600mg daily
   b. Patients at 600mg or less daily will be required to taper to 400mg daily

**Ultracet (tramadol and acetaminophen)**

**Age**

16 years of age or older

Patient must have the following:

Moderate to severe pain

**AND** the following:

1. Physician agrees to taper patient’s dose to the maximum FDA allowable dose based on their daily dose
   a. Patients taking over 600mg daily will be required to taper to 500mg daily
   b. Patients at 600mg or less daily will be required to taper to 300mg daily
Ultram ER and Conzip (tramadol ER)

Age 18 years of age or older

Patient must have the following:

Moderate to severe pain requiring daily, around-the-clock long term opioid treatment

AND the following:
2. Physician agrees to taper patient’s dose to the maximum FDA allowable dose based on their daily dose
   c. Patients taking over 600mg daily will be required to taper to 500mg daily
   a. Patients at 600mg or less daily will be required to taper to 300mg daily

Prior – Approval Renewal Requirements

Diagnosis

Ultram (tramadol)

Age 16 years of age or older

Patient must have the following:

Moderate to severe pain

AND the following:
1. Physician agrees to taper patient’s dose to the maximum FDA allowable dose of 400mg daily

Ultracet (tramadol and acetaminophen)

Age 16 years of age or older
Patient must have the following:

Moderate to severe pain

AND the following:
1. Physician agrees to taper patient’s dose to the maximum FDA allowable dose of 300mg daily

Ultram ER and Conzip (tramadol ER)

Age 18 years of age or older

Patient must have the following:

Moderate to severe pain requiring daily, around-the-clock long term opioid treatment

AND the following:
1. Physician agrees to taper patient’s dose to the maximum FDA allowable dose of 300mg daily

Policy Guidelines

Pre - PA Allowance

Quantity

Immediate-release Formulation

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Dosage Units per 90 days</th>
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<tr>
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<td>Ultram</td>
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Extended-release Formulations

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<td>Conzip</td>
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Prior - Approval Limits

Quantity

Immediate-release Formulation
### Section: Prescription Drugs

**Effective Date:** July 1, 2015

**Subsection:** Analgesics and Anesthetics

**Original Policy Date:** May 8, 2015

**Subject:** Tramadol

**Page:** 6 of 7

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**Above 600mg daily dose**

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**600mg or less daily dose**

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**Extended-release Formulations**

**Above 300mg daily dose**

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**300mg or less daily dose**

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**Duration**

6 months

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**Prior – Approval Renewal Limits**

**Immediate-release Formulation**

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<tr>
<td>Conzip</td>
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**Duration**

6 months - One renewal only for patients with an initial daily dose above 600mg
Rationale

Summary
Tramadol is a centrally acting synthetic opioid analgesic used to treat moderate to moderately severe chronic pain in adults. Concomitant use of serotonergic drugs such as SSRIs, SNRIs, TCAs, MAOIs, and SRAs (triptans) with tramadol may precipitate a potentially life-threatening condition called serotonin syndrome. The safety and efficacy of Ultram ER; Conzip in patients under 18 years of age have not been established (1,2). The safety and efficacy of Ultram in patients under 16 years of age has not been established. Ultracet is approved for short term use only. As with other opioids, all patients require monitoring for signs of abuse and addiction, as use of opioid analgesic products carries the risk of addiction even with appropriate medical care (1).

Prior approval is required to ensure the safe, clinically appropriate and cost effective use of Ultram, Ultram ER, and Conzip while maintaining optimal therapeutic outcomes.

References

Policy History

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<th>Date</th>
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<td>May 2015</td>
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This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 19, 2015 and is effective July 1, 2015.

Signature on file

Deborah M. Smith, MD, MPH