ULTRAM- tramadol hcl 50mg tablet, coated
Advanced Rx Pharmacy of Tennessee, LLC

Tramadol HCl 50mg tablets #120

Medication Guide Section

MEDICATION GUIDE

Tramadol Hydrochloride (tram' a dol hye" droe klor' ide) Tablets, USP CIV

Tramadol hydrochloride tablets are:

A strong prescription pain medicine that contains an opioid (narcotic) that is used for the management pain in adults, when other pain treatments such as non-opioid pain medicines do not treat your pain well enough or you cannot tolerate them.

An opioid pain medicine that can put you at risk for overdose and death. Even if you take your dose correctly as prescribed you are at risk for opioid addiction, abuse, and misuse that can lead to death.

Important information about tramadol hydrochloride tablets:

Get emergency help right away if you take too many tramadol hydrochloride tablets (overdose). When you first start taking tramadol hydrochloride tablets, when your dose is changed, or if you take too much (overdose), serious or life-threatening breathing problems that can lead to death may occur.
Taking tramadol hydrochloride tablets with other opioid medicines, benzodiazepines, alcohol, or other central nervous system depressants (including street drugs) can cause severe drowsiness, decreased awareness, breathing problems, coma, and death.

Never give anyone else your tramadol hydrochloride tablets. They could die from taking it. Selling or giving away tramadol hydrochloride tablets is against the law.
Store tramadol hydrochloride tablets securely, out of sight and reach of children, and in a location not accessible by others, including visitors to the home.

Important Information Guiding Use in Pediatric Patients:

Do not give tramadol hydrochloride tablets to a child younger than 12 years of age.
Do not give tramadol hydrochloride tablets to a child younger than 18 years of age after surgery to remove the tonsils and/or adenoids.
Avoid giving tramadol hydrochloride tablets to children between 12 to 18 years of age who have risk factors for breathing problems such as obstructive sleep apnea, obesity, or underlying lung problems.
Do not take tramadol hydrochloride tablets if you have:

Severe asthma, trouble breathing, or other lung problems.
A bowel blockage or have narrowing of the stomach or intestines.
An allergy to tramadol.

Taken a Monoamine Oxidase Inhibitor, MAOI, (medicine used for depression) within the last 14 days.

Before taking tramadol hydrochloride tablets, tell your healthcare provider if you have a

history of:

head injury, seizures

liver, kidney, thyroid problems

problems urinating

pancreas or gallbladder problems

abuse of street or prescription drugs, alcohol addiction, or mental health problems.

Tell your healthcare provider if you are:

pregnant or planning to become pregnant. Prolonged use of tramadol hydrochloride tablets during pregnancy can cause withdrawal symptoms in your newborn baby that could be life-threatening if not recognized and treated.
breastfeeding. Not recommended; it may harm your baby.
taking prescription or over-the-counter medicines, vitamins, or herbal supplements. Taking tramadol hydrochloride tablets with certain other medicines can cause serious side effects that could lead to death.

When taking tramadol hydrochloride tablets:

Do not change your dose. Take tramadol hydrochloride tablets exactly as prescribed by your healthcare provider. Use the lowest dose possible for the shortest time needed. Take your prescribed dose as indicated by your healthcare provider. The maximum dosage is 1 or 2 tablets every 4 to 6 hours, as needed for pain relief. Do not take more than your prescribed dose and do not take more than 8 tablets per day. If you miss a dose, take your next dose at your usual time.
Call your healthcare provider if the dose you are taking does not control your pain.
If you have been taking tramadol hydrochloride tablets regularly, do not stop taking tramadol hydrochloride tablets without talking to your healthcare provider.
Dispose of expired, unwanted, or unused tramadol hydrochloride tablets by taking your drug to an authorized Drug Enforcement Administration (DEA)-registered collector or drug take-back program. If one is not available, you can dispose of tramadol hydrochloride tablets by mixing the product with dirt, cat litter, or coffee grounds; placing the mixture in a sealed plastic bag, and throwing the bag in your trash.

While taking tramadol hydrochloride tablets DO NOT:

Drive or operate heavy machinery, until you know how tramadol hydrochloride tablets affect you. Tramadol hydrochloride tablets can make you sleepy, dizzy, or lightheaded.
Drink alcohol or use prescription or over-the-counter medicines that contain alcohol. Using products containing alcohol during treatment with tramadol hydrochloride tablets may cause you to overdose and die.

The possible side effects of tramadol hydrochloride tablets:

constipation, nausea, sleepiness, vomiting, tiredness, headache, dizziness, abdominal pain. Call your healthcare provider if you have any of these symptoms and they are severe.

Get emergency medical help if you have:

trouble breathing, shortness of breath, fast heartbeat, chest pain, swelling of your face, tongue, or throat, extreme drowsiness, light-headedness when changing positions,

feeling faint, agitation, high body temperature, trouble walking, stiff muscles, or mental changes such as confusion.

These are not all the possible side effects of tramadol hydrochloride tablets. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088. For more information go to dailymed.nlm.nih.gov.

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This Medication Guide has been approved by the U.S. Food and Drug Administration.

Dosage and Administration Section

2 DOSAGE AND ADMINISTRATION

2.1 Important Dosage and Administration Instructions

Do not use tramadol hydrochloride tablets concomitantly with other tramadol-containing products.
Do not administer tramadol hydrochloride tablets at a dose exceeding 400 mg per day.
Use the lowest effective dosage for the shortest duration consistent with individual patient treatment goals [see WARNINGS AND PRECAUTIONS (5.1)].
Initiate the dosing regimen for each patient individually, taking into account the patient's severity of pain, patient response, prior analgesic treatment experience, and risk factors for addiction, abuse, and misuse [see WARNINGS AND PRECAUTIONS (5.1)].
Monitor patients closely for respiratory depression, especially within the first 24 to 72 hours of initiating therapy and following dosage increases with tramadol hydrochloride tablets and adjust the dosage accordingly [see WARNINGS AND PRECAUTIONS (5.3)].

2.2 Initial Dosage

Initiating Treatment with Tramadol Hydrochloride Tablets

For patients not requiring rapid onset of analgesic effect, the tolerability of tramadol hydrochloride tablets can be improved by initiating therapy with the following titration regimen: Start tramadol hydrochloride tablets at 25 mg/day and titrated in 25 mg increments as separate doses every 3 days to reach 100 mg/day (25 mg four times a day). Thereafter the total daily dose may be increased by 50 mg as tolerated every 3 days to reach 200 mg/day (50 mg four times a day). After titration, tramadol hydrochloride tablets 50 mg to 100 mg can be administered as needed for pain relief every 4 to 6 hours not to exceed 400 mg/day.

For the subset of patients for whom rapid onset of analgesic effect is required and for whom the benefits outweigh the risk of discontinuation due to adverse events associated with higher initial doses, tramadol hydrochloride tablets 50 mg to 100 mg can

be administered as needed for pain relief every four to six hours, not to exceed 400 mg per day.

Conversion from Tramadol Hydrochloride Immediate-Release to Extended-Release Tramadol

The relative bioavailability of immediate-release tramadol hydrochloride compared to extended-release tramadol is unknown, so conversion to extended-release formulations must be accompanied by close observation for signs of excessive sedation and respiratory depression.

Dosage Modification in Patients with Hepatic Impairment

The recommended dose for adult patients with severe hepatic impairment is 50 mg every 12 hours.

Dosage Modification in Patients with Renal Impairment

In all patients with creatinine clearance less than 30 mL/min, it is recommended that the dosing interval of tramadol hydrochloride tablets be increased to 12 hours, with a maximum daily dose of 200 mg. Since only 7% of an administered dose is removed by hemodialysis, dialysis patients can receive their regular dose on the day of dialysis.

Dosage Modification in Geriatric Patients

Do not exceed a total dose of 300 mg/day in patients over 75 years old.

2.3 Titration and Maintenance of Therapy

Individually titrate tramadol hydrochloride tablets to a dose that provides adequate analgesia and minimizes adverse reactions. Continually re-evaluate patients receiving tramadol hydrochloride tablets to assess the maintenance of pain control and the relative incidence of adverse reactions, as well as to monitor for the development of addiction, abuse, or misuse [see WARNINGS AND PRECAUTIONS (5.1)]. Frequent communication is important among the prescriber, other members of the healthcare team, the patient, and the caregiver/family during periods of changing analgesic requirements, including initial titration.

If the level of pain increases after dosage stabilization, attempt to identify the source of increased pain before increasing the tramadol hydrochloride tablets dosage. If unacceptable opioid-related adverse reactions are observed, consider reducing the dosage. Adjust the dosage to obtain an appropriate balance between management of pain and opioid-related adverse reactions.

2.4 Safe Reduction or Discontinuation of Tramadol Hydrochloride Tablets

Do not abruptly discontinue tramadol hydrochloride tablets in patients who may be physically dependent on opioids. Rapid discontinuation of opioid analgesics in patients who are physically dependent on opioids has resulted in serious withdrawal symptoms, uncontrolled pain, and suicide. Rapid discontinuation has also been associated with attempts to find other sources of opioid analgesics, which may be confused with drug-seeking for abuse. Patients may also attempt to treat their pain or withdrawal symptoms with illicit opioids, such as heroin, and other substances.

When a decision has been made to decrease the dose or discontinue therapy in an opioid-dependent patient taking tramadol hydrochloride tablets, there are a variety of factors that should be considered, including the dose of tramadol hydrochloride tablets

the patient has been taking, the duration of treatment, the type of pain being treated, and the physical and psychological attributes of the patient. It is important to ensure ongoing care of the patient and to agree on an appropriate tapering schedule and follow-up plan so that patient and provider goals and expectations are clear and realistic. When opioid analgesics are being discontinued due to a suspected substance use disorder, evaluate and treat the patient, or refer for evaluation and treatment of the substance use disorder. Treatment should include evidence-based approaches, such as medication assisted treatment of opioid use disorder. Complex patients with comorbid pain and substance use disorders may benefit from referral to a specialist.

There are no standard opioid tapering schedules that are suitable for all patients. Good clinical practice dictates a patient-specific plan to taper the dose of the opioid gradually. For patients on tramadol hydrochloride tablets who are physically opioid-dependent, initiate the taper by a small enough increment, (e.g., no greater than 10% to 25% of the total daily dose) to avoid withdrawal symptoms, and proceed with dose-lowering at an interval of every 2 to 4 weeks. Patients who have been taking opioids for briefer periods of time may tolerate a more rapid taper.

It may be necessary to provide the patient with a lower dosage strength to accomplish a successful taper. Reassess the patient frequently to manage pain and withdrawal symptoms, should they emerge. Common withdrawal symptoms include restlessness, lacrimation, rhinorrhea, yawning, perspiration, chills, myalgia, and mydriasis. Other signs and symptoms also may develop, including irritability, anxiety, backache, joint pain, weakness, abdominal cramps, insomnia, nausea, anorexia, vomiting, diarrhea, or increased blood pressure, respiratory rate, or heart rate. If withdrawal symptoms arise, it may be necessary to pause the taper for a period of time or raise the dose of the opioid analgesic to the previous dose, and then proceed with a slower taper. In addition, monitor patients for any changes in mood, emergence of suicidal thoughts, or use of other substances.

When managing patients taking opioid analgesics, particularly those who have been treated for a long duration and/or with high doses for chronic pain, ensure that a multimodal approach to pain management, including mental health support (if needed), is in place prior to initiating an opioid analgesic taper. A multimodal approach to pain management may optimize the treatment of chronic pain, as well as assist with the successful tapering of the opioid analgesic [see WARNINGS AND PRECAUTIONS (5.17), DRUG ABUSE AND DEPENDENCE (9.3)].

Adverse Reactions Section

6 ADVERSE REACTIONS

The following serious adverse reactions are described, or described in greater detail, in other sections:

Addiction, Abuse, and Misuse [see WARNINGS AND PRECAUTIONS (5.1)]
Life-Threatening Respiratory Depression [see WARNINGS AND PRECAUTIONS (5.3)]
Ultra-Rapid Metabolism of Tramadol and Other Risk Factors for Life-threatening Respiratory Depression in Children [see WARNINGS AND PRECAUTIONS (5.4)]
Neonatal Opioid Withdrawal Syndrome [see WARNINGS AND PRECAUTIONS (5.5)]
Interactions with Benzodiazepines or Other CNS Depressants [see WARNINGS AND PRECAUTIONS (5.7)]

Serotonin Syndrome [see WARNINGS AND PRECAUTIONS (5.8)]
Seizures [see WARNINGS AND PRECAUTIONS (5.9)]
Suicide [see WARNINGS AND PRECAUTIONS (5.10)]
Adrenal Insufficiency [see WARNINGS AND PRECAUTIONS (5.11)]
Severe Hypotension [see WARNINGS AND PRECAUTIONS (5.13)]
Gastrointestinal Adverse Reactions [see WARNINGS AND PRECAUTIONS (5.15)]
Hypersensitivity Reactions [see WARNINGS AND PRECAUTIONS (5.16)]
Withdrawal [see WARNINGS AND PRECAUTIONS (5.17)]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Tramadol hydrochloride was administered to 550 patients during the double-blind or open-label extension periods in U.S. studies of chronic nonmalignant pain. Of these patients, 375 were 65 years old or older. Table 1 reports the cumulative incidence rate of adverse reactions by 7, 30 and 90 days for the most frequent reactions (5% or more by 7 days). The most frequently reported events were in the central nervous system and gastrointestinal system. Although the reactions listed in the table are felt to be probably related to tramadol hydrochloride administration, the reported rates also include some events that may have been due to underlying disease or concomitant medication. The overall incidence rates of adverse experiences in these trials were similar for tramadol hydrochloride and the active control groups, TYLENOL with Codeine #3 (acetaminophen 300 mg with codeine phosphate 30 mg), and aspirin 325 mg with codeine phosphate 30 mg, however, the rates of withdrawals due to adverse events appeared to be higher in the tramadol hydrochloride groups.

Table 1: Cumulative Incidence of Adverse Reactions for Tramadol Hydrochloride in Chronic Trials of Nonmalignant Pain (N=427)

Up to 7 Days

Up to 30 Days

Up to 90 Days

Dizziness/Vertigo

26%

31%

33%

Nausea

24%

34%

40%

Constipation

24%

38%

46%
Headache
18%
26%
32%
Somnolence
16%
23%
25%
Vomiting
9%
13%
17%
Pruritus
8%
10%
11%
“CNS Stimulation”1
7%
11%
14%
Asthenia
6%
11%
12%
Sweating
6%
7%
9%
Dyspepsia
5%
9%
13%

Dry Mouth

5%

9%

10%

Diarrhea

5%

6%

10%

1 “CNS Stimulation” is a composite of nervousness, anxiety, agitation, tremor, spasticity, euphoria, emotional lability and hallucinations

Incidence 1% to Less than 5% Possibly Causally Related

The following lists adverse reactions that occurred with an incidence of 1% to less than 5% in clinical trials, and for which the possibility of a causal relationship with tramadol hydrochloride exists.

Body as a Whole: Malaise.

Cardiovascular: Vasodilation.

Central Nervous System: Anxiety, Confusion, Coordination disturbance, Euphoria, Miosis, Nervousness, Sleep disorder.

Gastrointestinal: Abdominal pain, Anorexia, Flatulence.

Musculoskeletal: Hypertonia.

Skin: Rash.

Special Senses: Visual disturbance.

Urogenital: Menopausal symptoms, Urinary frequency, Urinary retention.

Incidence Less than 1%, Possibly Causally Related

The following lists adverse reactions that occurred with an incidence of less than 1% in clinical trials of tramadol and/or reported in postmarketing experience with tramadol-containing products.

Body as a Whole: Accidental injury, Allergic reaction, Anaphylaxis, Death, Suicidal tendency, Weight loss, Serotonin syndrome (mental status change, hyperreflexia, fever, shivering, tremor, agitation, diaphoresis, seizures and coma).

Cardiovascular: Orthostatic hypotension, Syncope, Tachycardia.

Central Nervous System: Abnormal gait, Amnesia, Cognitive dysfunction, Depression, Difficulty in concentration, Hallucinations, Paresthesia, Seizure, Tremor.

Respiratory: Dyspnea.

Skin: Stevens-Johnson syndrome/Toxic epidermal necrolysis, Urticaria, Vesicles.

Special Senses: Dysgeusia.

Urogenital: Dysuria, Menstrual disorder.

Other Adverse Experiences, Causal Relationship Unknown

A variety of other adverse events were reported infrequently in patients taking tramadol hydrochloride during clinical trials and/or reported in postmarketing experience. A causal relationship between tramadol hydrochloride and these events has not been determined. However, the most significant events are listed below as alerting information to the physician.

Cardiovascular: Abnormal ECG, Hypertension, Hypotension, Myocardial ischemia, Palpitations, Pulmonary edema, Pulmonary embolism.

Central Nervous System: Migraine.

Gastrointestinal: Gastrointestinal bleeding, Hepatitis, Stomatitis, Liver failure.

Laboratory Abnormalities: Creatinine increase, Elevated liver enzymes, Hemoglobin decrease, Proteinuria.

Sensory: Cataracts, Deafness, Tinnitus.

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of tramadol hydrochloride. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Serotonin syndrome: Cases of serotonin syndrome, a potentially life-threatening condition, have been reported during concomitant use of opioids with serotonergic drugs.

Adrenal insufficiency: Cases of adrenal insufficiency have been reported with opioid use, more often following greater than one month of use.

Androgen deficiency: Cases of androgen deficiency have occurred with chronic use of opioids [see CLINICAL PHARMACOLOGY (12.2)].

QT prolongation/torsade de pointes: Cases of QT prolongation and/or torsade de pointes have been reported with tramadol use. Many of these cases were reported in patients taking another drug labeled for QT prolongation, in patients with a risk factor for QT prolongation (e.g., hypokalemia), or in the overdose setting.

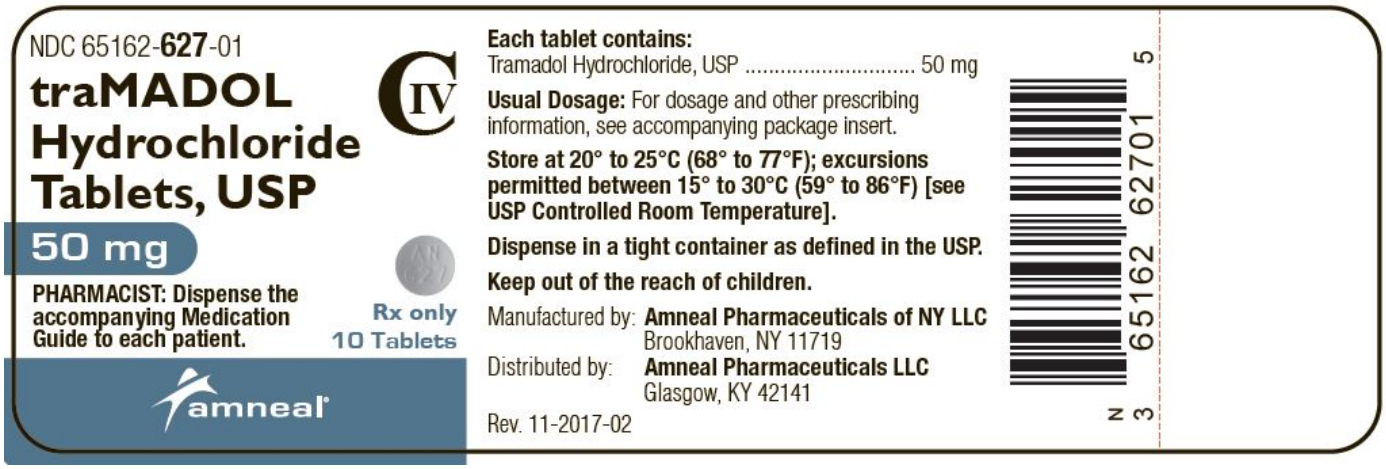
Eye disorders – mydriasis

Metabolism and nutrition disorders – Cases of hypoglycemia have been reported very rarely in patients taking tramadol. Most reports were in patients with predisposing risk factors, including diabetes or renal insufficiency, or in elderly patients.

Nervous system disorders – movement disorder, speech disorder

Psychiatric disorders – delirium

Principal Display Panel



ULTRAM

tramadol hcl 50mg tablet, coated

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:80425-0057(NDC:65162-627)
Route of Administration	ORAL	**DEA Schedule**	CIV

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
TRAMADOL HYDROCHLORIDE (UNII: 9N7R477WCK) (TRAMADOL - UNII:39J1LGJ30J)	TRAMADOL HYDROCHLORIDE	50 mg

Product Characteristics			
Color	white	**Score**	no score
Shape	ROUND	**Size**	9mm
Flavor		**Imprint Code**	AN;627
Contains			

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:80425-0057-5	120 in 1 BOTTLE; Type 0: Not a Combination Product	11/15/2010	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA076003	11/15/2010	

Labeler - Advanced Rx Pharmacy of Tennessee, LLC (117023142)

Establishment

Name	Address	ID/FEI	Business Operations
Advanced Rx Pharmacy of Tennessee, LLC		117023142	repack(80425-0057)

Revised: 4/2021 Advanced Rx Pharmacy of Tennessee, LLC