TRAMADOL HYDROCHLORIDE ER- tramadol hydrochloride tablet, extended release
H.J. Harkins Company, Inc.

1142-03,06

WARNING: ADDICTION, ABUSE, AND MISUSE; LIFE-THREATENING RESPIRATORY DEPRESSION; ACCIDENTAL INGESTION; ULTRA-RAPID METABOLISM OF TRAMADOL AND OTHER RISK FACTORS FOR LIFE-THREATENING RESPIRATORY DEPRESSION IN CHILDREN; NEONATAL OPIOID WITHDRAWAL SYNDROME; INTERACTIONS WITH DRUGS AFFECTING CYTOCHROME P450 ISOENZYMES; AND RISKS FROM CONCOMITANT USE WITH BENZODIAZEPINES OR OTHER CNS DEPRESSANTS
SEE FULL PRESCRIBING INFORMATION FOR COMPLETE BOXED WARNING.

Tramadol hydrochloride extended-release tablets expose users to risks of addiction, abuse, and misuse, which can lead to overdose and death. Assess patient's risk before prescribing and monitor regularly for these behaviors and conditions. (5.1)
Serious, life-threatening, or fatal respiratory depression may occur. Monitor closely, especially upon initiation or following a dose increase. Instruct patients to swallow tramadol hydrochloride extended-release tablets intact, and not to cut, break, chew, crush, or dissolve the tablets to avoid exposure to a potentially fatal dose of tramadol. (5.2)
Accidental ingestion of tramadol hydrochloride extended-release tablets, especially by children, can result in a fatal overdose of tramadol. (5.2)
Life-threatening respiratory depression and death have occurred in children who received tramadol. Some of the reported cases followed tonsillectomy and/or adenoidectomy; in at least one case, the child had evidence of being an ultra-rapid metabolizer of tramadol due to a CYP2D6 polymorphism (5.3). Tramadol hydrochloride extended-release tablets are contraindicated in children younger than 12 years of age and in children younger than 18 years of age following tonsillectomy and/or adenoidectomy (4). Avoid the use of tramadol hydrochloride extended-release tablets in adolescents 12 to 18 years of age who have other risk factors that may increase their sensitivity to the respiratory depressant effects of tramadol. [see Warnings and Precautions (5.3)]
Prolonged use of tramadol hydrochloride extended-release tablets during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated. If prolonged opioid use is required in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available. (5.4)
The effects of concomitant use or discontinuation of cytochrome P450 3A4 inducers, 3A4 inhibitors, or 2D6 inhibitors with tramadol are complex. Use of cytochrome P450 3A4 inducers, 3A4 inhibitors, or 2D6 inhibitors with tramadol hydrochloride extended-release tablets requires careful consideration of the effects on the parent drug, tramadol, and the active metabolite, M1 (5.5, 7)
Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death. Reserve concomitant prescribing for use in patients for whom alternative treatment options are inadequate; limit dosages and durations to the minimum required; and follow patients for signs and symptoms of respiratory depression and sedation. (5.6, 7)

Tramadol hydrochloride is an opioid agonist 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)
Limitations of Use

Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release opioid formulations, reserve tramadol hydrochloride extended-release tablets for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain. (1)
Tramadol hydrochloride extended-release tablets are not indicated as an as-needed (prn) analgesic. (1)

To be prescribed only by healthcare providers knowledgeable in use of potent opioids for management of chronic pain. (2.1)
Use the lowest effective dosage for the shortest duration consistent with individual patient treatment goals (2.1).
Individualize dosing based on the severity of pain, patient response, prior analgesic experience, and risk factors for addiction, abuse, and misuse. (2.1)
Do not exceed a daily dose of 300 mg tramadol. Do not use with other tramadol products.(2.1)
For opioid-naïve and opioid non-tolerant patients, initiate tramadol hydrochloride extended-release tablets at a dose of 100 mg once daily, then titrate up by 100 mg increments every 5 days according to need and tolerance. (2.2)
For patients currently on tramadol IR, calculate total 24-hr IR dose, and initiate tramadol hydrochloride extended-release tablets at a dose rounded down to next lower 100 mg increment; then adjust dose according to need and tolerance. See full prescribing information for instructions on conversion, titration, and maintenance of therapy. (2.2, 2.3)
Do not abruptly discontinue tramadol hydrochloride extended-release tablets in a physically-dependent patient. (2.4)

Children younger than 12 years of age (4)
Postoperative management in children younger than 18 years of age following tonsillectomy and/or adenoidectomy. (4)
Significant respiratory depression (4)
Acute or severe bronchial asthma in an unmonitored setting or in absence of resuscitative equipment (4)
Known or suspected gastrointestinal obstruction, including paralytic ileus (4)
Hypersensitivity to tramadol (4)
Concurrent use of monoamine oxidase inhibitors (MAOIs) or use within the last 14 days (4)

Serotonin Syndrome: Potentially life-threatening condition could result from concomitant serotonergic drug administration. Discontinue tramadol hydrochloride extended-release tablets if serotonin syndrome is suspected. (5.7)
Risk of Seizure: Present within recommended dosage range. Risk is increased with higher than recommended doses and concomitant use of SSRIs, SNRIs, anorectics, tricyclic antidepressants and other tricyclic compounds, other opioids, MAOIs, neuroleptics, other drugs that reduce seizure threshold, in patients with epilepsy or at risk for seizures. (5.8, 7)
Risk of Suicide: Do not use tramadol hydrochloride extended-release tablets in suicidal or addiction-prone patients. Use with caution in those taking tranquilizers, antidepressants or abuse alcohol. (5.9)
Adrenal Insufficiency: If diagnosed, treat with physiologic replacement of corticosteroids, and wean patient off of the opioid. (5.10)
Life-Threatening Respiratory Depression in Patients with Chronic Pulmonary Disease or in Elderly, Cachectic, or Debilitated Patients: Monitor closely, particularly during initiation and titration. (5.11)
Severe Hypotension: Monitor during dosage initiation and titration. Avoid use of tramadol hydrochloride extended-release tablets in patients with circulatory shock. (5.12)
Risks of Use in Patients with Increased Intracranial Pressure, Brain Tumors, Head Injury, or Impaired Consciousness: Monitor for sedation and respiratory depression. Avoid use of tramadol hydrochloride extended-release tablets in patients with impaired consciousness or coma. (5.13)

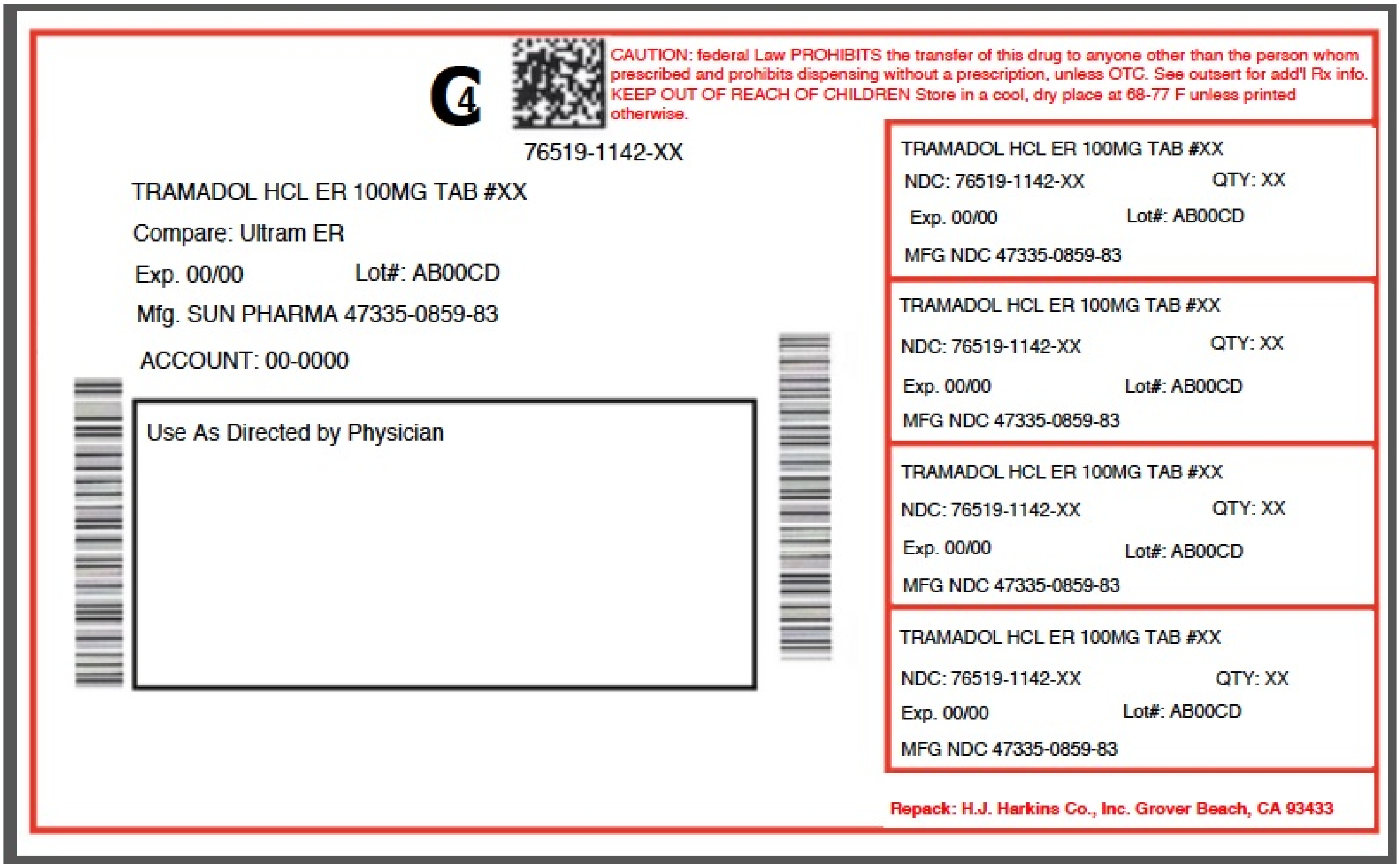
Most common adverse reactions (≥10% and ≥2 x placebo rate): Dizziness, constipation, nausea, headache, somnolence, flushing, pruritus, vomiting, insomnia, dry mouth. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact FDA at 1-800-FDA-1088 or

www.fda.gov/medwatch.

Mixed Agonist/Antagonist and Partial Agonist Opioid Analgesics: Avoid use with tramadol hydrochloride extended-release tablets because they may reduce analgesic effect of tramadol hydrochloride extended-release tablets or precipitate withdrawal symptoms. (5.16,7)

Advise the patient to read the FDA-approved patient labeling (Medication Guide).



TRAMADOL HYDROCHLORIDE ER

tramadol hydrochloride tablet, extended release

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:76519-1142
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	100 mg

Product Characteristics			
Color	white	**Score**	no score
Shape	ROUND	**Size**	8mm
Flavor		**Imprint Code**	531
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:76519-1142-3	30 in 1 VIAL, PLASTIC; Type 0: Not a Combination Product	07/15/2016	
2	NDC:76519-1142-6	60 in 1 VIAL, PLASTIC; Type 0: Not a Combination Product	07/15/2016	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA201384	07/15/2016	

Labeler - H.J. Harkins Company, Inc. (147681894)

Establishment

Name	Address	ID/FEI	Business Operations
H.J. Harkins Company, Inc.		147681894	relabel(76519-1142) , repack(76519-1142) , manufacture(76519-1142)

Revised: 8/2018 H.J. Harkins Company, Inc.