ANDA 75-983
Tramadol Hydrochloride Tablets, 50 mg

Final Printed Labeling

Label for Unit Dose Carton (100 Tablets [10x10])

NDC 0406-7171-62

TRAMADOL HYDROCHLORIDE

TABLETS

50 mg

100 Tablets (10x10)

0406717162

NDC 0406-7171-62

TRAMADOL HYDROCHLORIDE

TABLETS

50 mg

100 Tablets (10x10)

Rx only

Each tablet contains:
Tramadol Hydrochloride ..... 50 mg

USUAL DOSAGE:
See package insert for complete dosage recommendations.

STORAGE: Store at controlled room temperature 15° to 30°C (59° to 86°F) [See USP]. Keep tablets in box to protect from light.

Mallinckrodt Inc.
St. Louis, Missouri
63134, U.S.A.

110239
Rev. 12/2001

ANDA 75-983
Tramadol Hydrochloride Tablets, 50 mg

Final Printed Labeling

Unit Dose Carton

USUAL DOSAGE:
See package insert for complete dosage recommendations.

See label for temperature storage conditions.

This product is protected with sealed blister units. Do not use if any are torn or broken.

This unit-dose package is not child resistant.
See window for expiration date and lot number.

Mallinckrodt

UNIT-DOSE

SPECIMEN

tyco / Healthcare

APPROVED

ANDA 75-983
Tramadol Hydrochloride Tablets, 50 mg

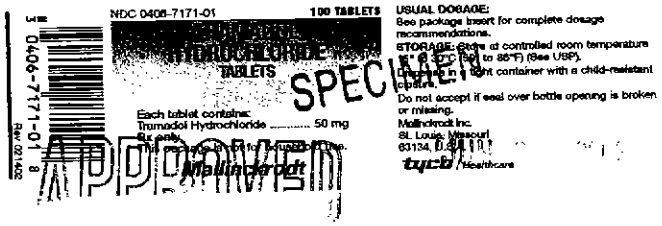
Final Printed Labeling

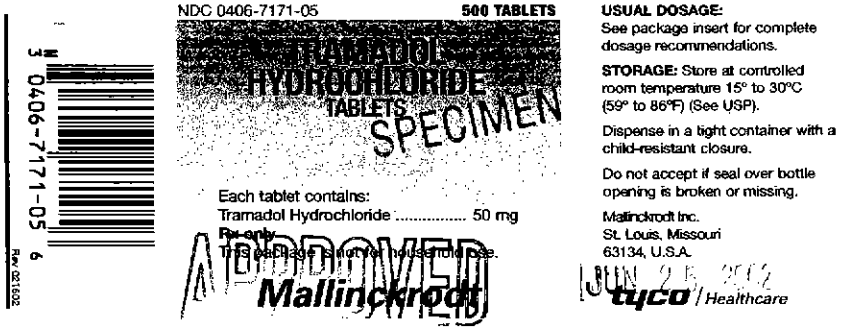
Label for Unit Dose

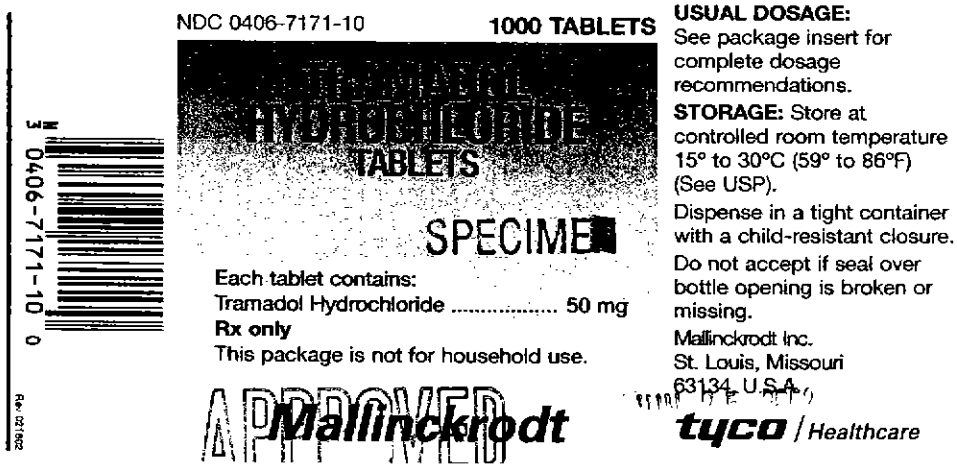
ANDA 75-983
Tramadol Hydrochloride Tablets, 50 mg

Final Printed Labeling

100-Count, 500-Count and 1000-Count Bottle Labels







ANDA 75-983
Tramadol Hydrochloride Tablets, 50 mg

Final Printed Labeling

Package Insert

Geriatric Use

In general, dose selection for an elderly patient should be cautious, usually starting at the lower end of the dosing range, reflecting the greater frequency of decreased hepatic, renal or cardiac function and of concomitant disease or other drug therapy. In patients over 75 years of age, daily doses in excess of 300 mg are not recommended. (see CLINICAL PHARMACOLOGY and DOSAGE AND ADMINISTRATION)

A total of 455 elderly (65 years of age or older) subjects were exposed to tramadol in controlled clinical trials. Of those, 145 subjects were 75 years of age and older. In studies including geriatric patients, treatment-limiting adverse events were higher in subjects over 75 years of age compared to those under 65 years of age. Specifically, 30% of those over 75 years of age had gastrointestinal treatment-limiting adverse events compared to 17% of those under 65 years of age. Constipation resulted in discontinuation of treatment in 10% of those over 75.

ADVERSE REACTIONS

Tramadol 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 2 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 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 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 groups.

Table 2: Cumulative Incidence of Adverse Reactions for Tramadol in Chronic Trials of Nonmalignant Pain (N=427)

	Up to 7 Days	Up to 30 Days	Up to 90 Days

Cardiovascular: Abnormal ECG, Hypertension, Hypotension, Myocardial ischemia, Palpitations, Pulmonary edema, Pulmonary embolism.
Central Nervous System: Migraine, Speech disorders.
Gastrointestinal: Gastroimestinal bleeding, Hepatitis, Stomatitis, Liver failure.
Laboratory Abnormalities: Creatinine increase, Elevated liver enzymes, Hemoglobin decrease, Proteinuria.
Sensory: Cataracts, Deafness, Tinnitus.

DRUG ABUSE AND DEPENDENCE

Tramadol may induce psychic and physical dependence of the morphine-type (μ-opioid) (See WARNINGS). Dependence and abuse, including drug-seeking behavior and taking illicit actions to obtain the drug are not limited to those patients with prior history of opioid dependence. The risk in patients with substance abuse has been observed to be higher. Tramadol is associated with craving and tolerance development. Withdrawal symptoms may occur if tramadol is discontinued abruptly. These symptoms may include: anxiety, sweating, insomnia, rigors, pain, nausea, tremors, diarrhea, upper respiratory symptoms, pilоerection, and rarely hallucinations. Clinical experience suggests that withdrawal symptoms may be relieved by reinstitution of opioid therapy followed by a gradual, tapered dose reduction of the medication combined with symptomatic support.

OVERDOSAGE

Serious potential consequences of overdosage are respiratory depression, lethargy, coma, seizure, cardiac arrest and death. (See WARNINGS). Fatalities have been reported in post marketing in association with both intentional and unintentional overdose with tramadol. In treating an overdose, primary attention should be given to maintaining adequate ventilation along with general supportive treatment. While naloxone will reverse some, but not all, symptoms caused by overdosage with tramadol the risk of seizures is also increased with naloxone administration. In animals convulsions following the administration of toxic doses of tramadol could be suppressed with barbiturates or benzodiazepines but were increased with naloxone. Naloxone administration did not change the lethality of an overdose in mice. Hemodialysis is not expected to be helpful in an overdose because it removes less than 7% of the administered dose in a 4-hour dialysis period.

DOSAGE AND ADMINISTRATION