9.3 Dependence

Tolerance is the need for increasing doses of opioids to maintain a defined effect such as analgesia (in the absence of disease progression or other external factors). Physical dependence is manifested by withdrawal symptoms after abrupt discontinuation of a drug or upon administration of an antagonist.

The opioid abstinence or withdrawal syndrome is characterized by some or all of the following: restlessness, lacrimation, rhinorrhea, yawning, perspiration, chills, myalgia, and mydriasis. Other symptoms also may develop, including irritability, anxiety, backache, joint pain, weakness, abdominal cramps, insomnia, nausea, anorexia, vomiting, diarrhea, increased blood pressure, respiratory rate, or heart rate.

Generally, tolerance and/or withdrawal are more likely to occur the longer a patient is on continuous opioid therapy. In a safety study where drug was administered up to 90 days, 82.7% of patients taking TRADENAME™ who stopped abruptly without initiating alternative therapy and were assessed 2 to 4 days after discontinuation, did not have objective signs of opioid withdrawal using the Clinical Opiate Withdrawal Scale. Moderate withdrawal symptoms were seen in 0.3% of patients with the rest (17%) experiencing mild symptoms. Withdrawal symptoms may be reduced by tapering TRADENAME™.

10 OVERDOSAGE

10.1 Human Experience

Experience with TRADENAME™ overdose is very limited. Preclinical data suggest that symptoms similar to those of other centrally acting analgesics with mu-opioid agonist activity are to be expected upon intoxication with tapentadol. In principle, these symptoms may particularly appear in the clinical setting: miosis, vomiting, cardiovascular collapse, consciousness disorders up to coma, convulsions and respiratory depression up to respiratory arrest.

10.2 Management of Overdose

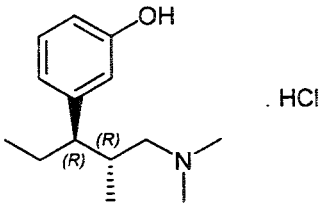
Management of overdose should be focused on treating symptoms of mu-opioid agonism. Primary attention should be given to re-establishment of a patent airway and institution of assisted or controlled ventilation when overdose of TRADENAME™ is suspected. Supportive measures (including oxygen and vasopressors) should be employed in the management of circulatory shock and pulmonary edema accompanying overdose as indicated. Cardiac arrest or arrhythmias may require cardiac massage or defibrillation.

Pure opioid antagonists, such as naloxone, are specific antidotes to respiratory depression resulting from opioid overdose. Respiratory depression following an overdose may outlast the duration of action of the opioid antagonist. Administration of an opioid antagonist is not a substitute for continuous monitoring of airway, breathing, and circulation following an opioid overdose. If the response to opioid antagonists is suboptimal or only brief in nature, an additional antagonist should be administered as directed by the manufacturer of the product.

Gastrointestinal decontamination may be considered in order to eliminate unabsorbed drug. Gastrointestinal decontamination with activated charcoal or by gastric lavage is only recommended within 2 hours after intake. Gastrointestinal decontamination at a later time point may be useful in case of intoxication with exceptionally large quantities. Before attempting gastrointestinal decontamination, care should be taken to secure the airway.

11 DESCRIPTION

TRADENAME™ (tapentadol) Tablets are immediate-release film-coated tablets for oral administration. The chemical name is 3-[(1*R*,2*R*)-3-(dimethylamino)-1-ethyl-2-methylpropyl]phenol monohydrochloride. The structural formula is:



The molecular weight of tapentadol HCl is 257.80, and the molecular formula is $C_{14}H_{23}NO \cdot HCl$. The n-octanol:water partition coefficient log P value is 2.87. The pKa values are 9.34 and 10.45. In addition to the active ingredient tapentadol HCl, tablets also contain the following inactive ingredients: microcrystalline cellulose, lactose monohydrate, croscarmellose sodium, povidone, magnesium stearate, and Opadry® II, a proprietary film-coating mixture containing polyvinyl alcohol, titanium dioxide, polyethylene glycol, talc, and aluminum lake coloring.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Tapentadol is a centrally-acting synthetic analgesic. Although its exact mechanism is unknown, analgesic efficacy is thought to be due to mu-opioid agonist activity and the inhibition of norepinephrine reuptake.

12.2 Pharmacodynamics

Tapentadol is a centrally-acting synthetic analgesic. It is 18 times less potent than morphine in binding to the human mu-opioid receptor and is 2-3 times less potent in producing analgesia in animal models. Tapentadol has been shown to inhibit norepinephrine reuptake in the brains of rats resulting in increased norepinephrine concentrations. In preclinical models, the analgesic activity due to the mu-opioid receptor agonist activity of tapentadol can be antagonized by selective mu-opioid antagonists (e.g., naloxone), whereas the norepinephrine reuptake inhibition is sensitive to norepinephrine modulators. Tapentadol exerts its analgesic effects without a pharmacologically active metabolite.

Effects on the cardiovascular system: There was no effect of therapeutic and supratherapeutic doses of tapentadol on the QT interval. In a randomized, double-blind, placebo- and positive-controlled crossover study, healthy subjects were administered five consecutive doses of

TRADENAME™ 100 mg every 6 hours, TRADENAME™ 150 mg every 6 hours, placebo and a single oral dose of moxifloxacin. Similarly, TRADENAME™ had no relevant effect on other ECG parameters (heart rate, PR interval, QRS duration, T-wave or U-wave morphology).

12.3 Pharmacokinetics

Absorption

Mean absolute bioavailability after single-dose administration (fasting) is approximately 32% due to extensive first-pass metabolism. Maximum serum concentrations of tapentadol are typically observed at around 1.25 hours after dosing.

Dose-proportional increases in the C_{max} and AUC values of tapentadol have been observed over the 50 to 150 mg dose range.

A multiple (every 6 hour) dose study with doses ranging from 75 to 175 mg tapentadol showed a mean accumulation factor of 1.6 for the parent drug and 1.8 for the major metabolite tapentadol-O-glucuronide, which are primarily determined by the dosing interval and apparent half-life of tapentadol and its metabolite.

Food Effect

The AUC and C_{max} increased by 25% and 16%, respectively, when TRADENAME™ was administered after a high-fat, high-calorie breakfast. TRADENAME™ may be given with or without food.

Distribution

Tapentadol is widely distributed throughout the body. Following intravenous administration, the volume of distribution (Vz) for tapentadol is 540 +/- 98 L. The plasma protein binding is low and amounts to approximately 20%.

Metabolism and Elimination

In humans, the metabolism of tapentadol is extensive. About 97% of the parent compound is metabolized. Tapentadol is mainly metabolized via Phase 2 pathways, and only a small amount is metabolized by Phase 1 oxidative pathways. The major pathway of tapentadol metabolism is conjugation with glucuronic acid to produce glucuronides. After oral administration approximately 70% (55% O-glucuronide and 15% sulfate of tapentadol) of the dose is excreted in urine in the conjugated form. A total of 3% of drug was excreted in urine as unchanged drug. Tapentadol is additionally metabolized to N-desmethyl tapentadol (13%) by CYP2C9 and CYP2C19 and to hydroxy tapentadol (2%) by CYP2D6, which are further metabolized by conjugation. Therefore, drug metabolism mediated by cytochrome P450 system is of less importance than phase 2 conjugation.

None of the metabolites contributes to the analgesic activity.

Tapentadol and its metabolites are excreted almost exclusively (99%) via the kidneys. The terminal half-life is on average 4 hours after oral administration. The total clearance is 1530 +/- 177 ml/min.

Special Populations

Elderly

The mean exposure (AUC) to tapentadol was similar in elderly subjects compared to young adults, with a 16% lower mean C_{max} observed in the elderly subject group compared to young adult subjects.

Renal Impairment

AUC and C_{max} of tapentadol were comparable in subjects with varying degrees of renal function (from normal to severely impaired). In contrast, increasing exposure (AUC) to tapentadol-O-glucuronide was observed with increasing degree of renal impairment. In subjects with mild, moderate, and severe renal impairment, the AUC of tapentadol-O-glucuronide are 1.5-, 2.5-, and 5.5-fold higher compared with normal renal function, respectively.

Hepatic Impairment

Administration of TRADENAME™ resulted in higher exposures and serum levels to tapentadol in subjects with impaired hepatic function compared to subjects with normal hepatic function. The ratio of tapentadol pharmacokinetic parameters for the mild and moderate hepatic impairment groups in comparison to the normal hepatic function group were 1.7 and 4.2, respectively, for AUC; 1.4 and 2.5, respectively, for C_{max}; and 1.2 and 1.4, respectively, for $t_{1/2}$. The rate of formation of tapentadol-O-glucuronide was lower in subjects with increased liver impairment.

Pharmacokinetic Drug Interactions

Tapentadol is mainly metabolized by Phase 2 glucuronidation, a high capacity/low affinity system, therefore, clinically relevant interactions caused by Phase 2 metabolism are unlikely to occur. Naproxen and probenecid increased the AUC of tapentadol by 17% and 57%, respectively. These changes are not considered clinically relevant and no change in dose is required.

No changes in the pharmacokinetic parameters of tapentadol were observed when acetaminophen and acetylsalicylic acid were given concomitantly.

In vitro studies did not reveal any potential of tapentadol to either inhibit or induce cytochrome P450 enzymes. Thus, clinically relevant interactions mediated by the cytochrome P450 system are unlikely to occur.

The pharmacokinetics of tapentadol were not affected when gastric pH or gastrointestinal motility were increased by omeprazole and metoclopramide, respectively.

Plasma protein binding of tapentadol is low (approximately 20%). Therefore, the likelihood of pharmacokinetic drug-drug interactions by displacement from the protein binding site is low.

13 NON-CLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Tapentadol was administered to rats (diet) and mice (oral gavage) for two years.

In mice, tapentadol HCl was administered by oral gavage at dosages of 50, 100 and 200 mg/kg/day for 2 years (up to 0.2 times the plasma exposure at the maximum recommended human dose [MRHD] on an area under the time-curve [AUC] basis). No increase in tumor incidence was observed at any dose level.

In rats, tapentadol HCl was administered in diet at dosages of 10, 50, 125 and 250 mg/kg/day for two years (up to 0.2 times in the male rats and 0.6 times in the female rats the MRHD on an AUC basis). No increase in tumor incidence was observed at any dose level.

Mutagenesis

Tapentadol did not induce gene mutations in bacteria, but was clastogenic with metabolic activation in a chromosomal aberration test in V79 cells. The test was repeated and was negative in the presence and absence of metabolic activation. The one positive result for tapentadol was not confirmed *in vivo* in rats, using the two endpoints of chromosomal aberration and unscheduled DNA synthesis, when tested up to the maximum tolerated dose.

Impairment of Fertility

Tapentadol HCl was administered intravenously to male or female rats at dosages of 3, 6, or 12 mg/kg/day (representing exposures of up to approximately 0.4 times the exposure at the MRHD on an AUC basis, based on extrapolation from toxicokinetic analyses in a separate 4-week intravenous study in rats). Tapentadol did not alter fertility at any dose level. Maternal toxicity and adverse effects on embryonic development, including decreased number of implantations, decreased numbers of live conceptuses, and increased pre- and post-implantation losses occurred at dosages ≥6 mg/kg/day.

13.2 Animal Toxicology and/or Pharmacology

In toxicological studies with tapentadol, the most common systemic effects of tapentadol were related to the mu-opioid receptor agonist and norepinephrine reuptake inhibition pharmacodynamic properties of the compound. Transient, dose-dependent and predominantly CNS-related findings were observed, including impaired respiratory function and convulsions, the latter occurring in the dog at plasma levels (C_{max}) which are in the range associated with the maximum recommended human dose (MRHD).

14 CLINICAL STUDIES

The efficacy and safety of TRADENAME™ in the treatment of moderate to severe acute pain has been established in two randomized, double-blind, placebo- and active-controlled studies of

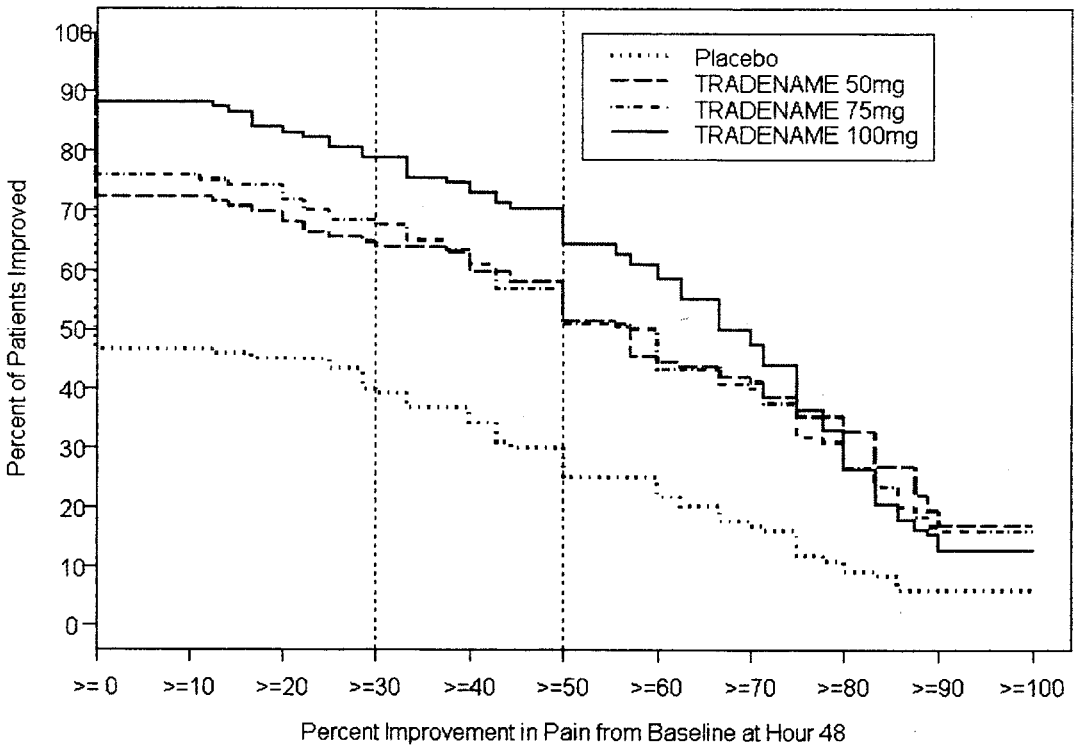
moderate to severe pain from first metatarsal bunionectomy and end-stage degenerative joint disease.

14.1 Orthopedic Surgery – Bunionectomy

A randomized, double-blind, parallel-group, active- and placebo-controlled, multiple-dose study demonstrated the efficacy of 50 mg, 75 mg, and 100 mg TRADENAME™ given every 4 to 6 hours for 72 hours in patients aged 18 to 80 years experiencing moderate to severe pain following unilateral, first metatarsal bunionectomy surgery. Patients who qualified for the study with a baseline pain score of $\geq$4 on an 11-point rating scale ranging from 0 to 10 were randomized to 1 of 5 treatments. Patients were allowed to take a second dose of study medication as soon as 1 hour after the first dose on study Day 1, with subsequent dosing every 4 to 6 hours. If rescue analgesics were required, the patients were discontinued for lack of efficacy. Efficacy was evaluated by comparing the sum of pain intensity difference over the first 48 hours (SPID48) versus placebo. TRADENAME™ at each dose provided a greater reduction in pain compared to placebo based on SPID48 values.

For various degrees of improvement from baseline to the 48-hour endpoint, Figure 1 shows the fraction of patients achieving that level of improvement. The figures are cumulative, such that every patient that achieves a 50% reduction in pain from baseline is included in every level of improvement below 50%. Patients who did not complete the 48-hour observation period in the study were assigned 0% improvement.

Figure 1: Percentage of Patients Achieving Various Levels of Pain Relief as Measured by Pain Severity at 48 Hours Compared to Baseline- Post Operative Bunionectomy



The proportions of patients who showed reduction in pain intensity at 48 hours of 30% or greater, or 50% or greater were significantly higher in patients treated with TRADENAME™ at each dose versus placebo.

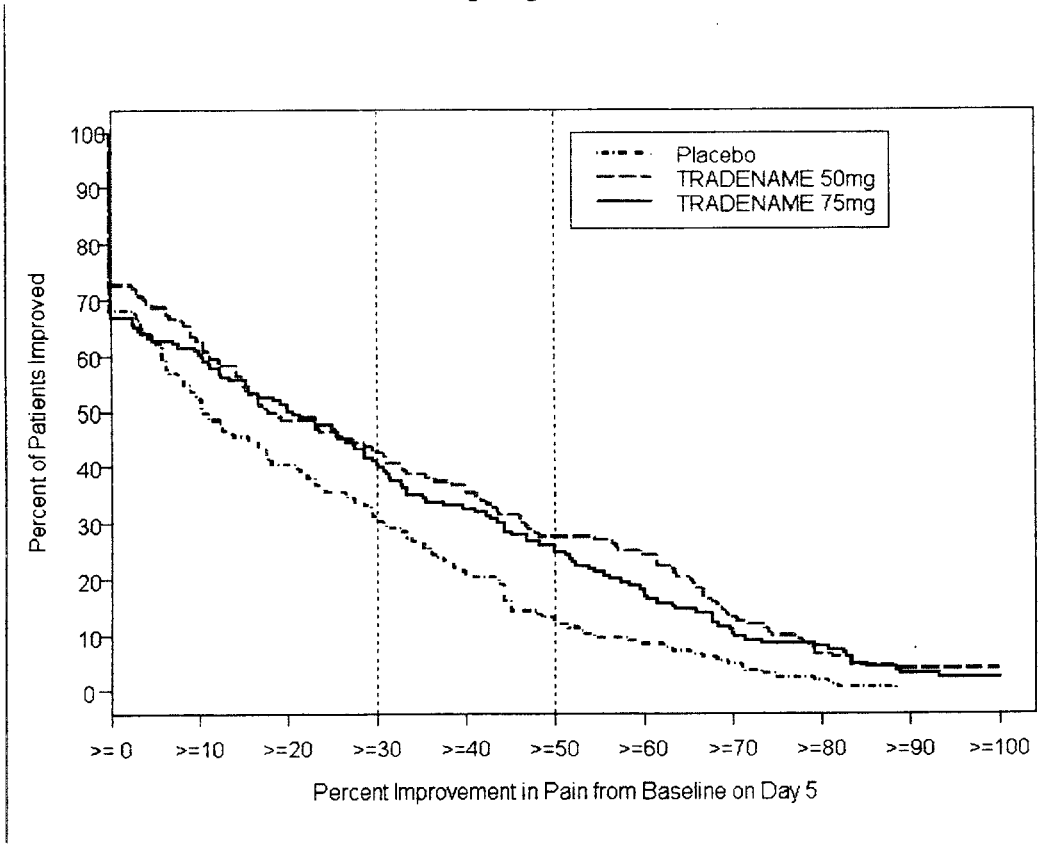
14.2 End-Stage Degenerative Joint Disease

A randomized, double-blind, parallel-group, active- and placebo-controlled, multiple-dose study evaluated the efficacy and safety of 50 mg and 75 mg TRADENAME™ given every 4 to 6 hours during waking hours for 10 days in patients aged 18 to 80 years, experiencing moderate to severe pain from end stage degenerative joint disease of the hip or knee, defined as a 3-day mean pain score of ≥5 on an 11-point pain intensity scale, ranging from 0 to 10. Pain scores were assessed twice daily and assessed the pain the patient had experienced over the previous 12 hours. Patients were allowed to continue non-opioid analgesic therapy for which they had been on a stable regimen before screening throughout the study. Eighty-three percent (83%) of patients in the tapentadol treatment groups and the placebo group took such analgesia during the study. The 75 mg treatment group was dosed at 50 mg for the first day of the study, followed by 75 mg for the remaining nine days. Patients requiring rescue analgesics other than study medication were discontinued for lack of efficacy. Efficacy was evaluated by comparing the sum of pain intensity

difference (SPID) versus placebo over the first five days of treatment. TRADENAME™ 50 mg and 75 mg provided improvement in pain compared with placebo based on the 5-Day SPID.

For various degrees of improvement from baseline to the Day 5 endpoint, Figure 2 shows the fraction of patients achieving that level of improvement. The figures are cumulative, such that every patient that achieves a 50% reduction in pain from baseline is included in every level of improvement below 50%. Patients who did not complete the 5-day observation period in the study were assigned 0% improvement.

Figure 2: Percentage of Patients Achieving Various Levels of Pain Relief as Measured by Average Pain Severity for the Previous 12 hours, Measured on Study Day 5 Compared to Baseline -- End Stage Degenerative Joint Disease



The proportions of patients who showed reduction in pain intensity at 5 days of 30% or greater, or 50% or greater were significantly higher in patients treated with TRADENAME™ at each dose versus placebo.

16 HOW SUPPLIED/STORAGE AND HANDLING

TRADENAME™ Tablets are available in the following strengths and packages. All tablets are round and biconvex-shaped.

50 mg tablets are yellow and debossed with "O-M" on one side and "50" on the other side, and are available in bottles of 100 (NDC 50458-820-04) and hospital unit dose blister packs of 10 (NDC 50458-820-02).

75 mg tablets are yellow-orange and debossed with "O-M" on one side and "75" on the other side, and are available in bottles of 100 (NDC 50458-830-04) and hospital unit dose blister packs of 10 (NDC 50458-830-02).

100 mg tablets are orange and debossed with "O-M" on one side and "100" on the other side, and are available in bottles of 100 (NDC 50458-840-04) and hospital unit dose blister packs of 10 (NDC 50458-840-02).

Store up to 25°C (77°F); excursions permitted to 15 - 30°C (59 - 86°F) [see USP Controlled Room Temperature]. Protect from moisture.

Keep out of reach of children.

17 PATIENT COUNSELING INFORMATION

Physicians are advised to discuss the following issues with patients for whom they prescribe TRADENAME™:

17.1 Instructions for Use

Patients should be advised TRADENAME™ should be taken only as directed and to report episodes of breakthrough pain and adverse experiences occurring during therapy to their physician. Individualization of dosage is essential to make optimal use of this medication. Patients should be advised not to adjust the dose of TRADENAME™ without consulting their physician *[see Dosage and Administration (2)]*. Patients should be advised that it may be appropriate to taper dosing when discontinuing treatment with TRADENAME™ as withdrawal symptoms may occur *[see Drug Abuse and Dependence (9.3)]*. The physician can provide a dose schedule to accomplish a gradual discontinuation of the medication.

17.2 Misuse and Abuse

Patients should be advised that TRADENAME™ is a potential drug of abuse. Patients should protect TRADENAME™ from theft, and TRADENAME™ should never be given to anyone other than the individual for whom TRADENAME™ was prescribed *[see Warnings and Precautions (5.4)]*.

17.3 Interference with Cognitive and Motor Performance

As TRADENAME™ has the potential to impair judgment, thinking, or motor skills, patients should be cautioned about operating hazardous machinery, including automobiles *[see Warnings and Precautions (5.5)]*.

17.4 Pregnancy

Patients should be advised to notify their physician if they become pregnant or intend to become pregnant during treatment with TRADENAME™ *[see Use in Specific Populations (8.1)]*.

17.5 Nursing

Patients should be advised not to breast-feed an infant during treatment with TRADENAME™ *[see Use in Specific Populations (8.3)]*.

17.6 Monoamine Oxidase Inhibitors

Patients should be informed not to take TRADENAME™ while using any drugs that inhibit monoamine oxidase. Patients should not start any new medications while taking TRADENAME™ until they are assured by their healthcare provider that the new medication is not a monoamine oxidase inhibitor.

17.7 Seizures

Patients should be informed that TRADENAME™ could cause seizures if they are at risk for seizures or have epilepsy. Such patients should be advised to use TRADENAME™ with care *[see Warnings and Precautions (5.7)]*. Patients should be advised to stop taking TRADENAME™ if they have a seizure while taking TRADENAME™ and call their healthcare provider right away.

17.8 Serotonin Syndrome

Patients should be informed that TRADENAME™ could cause rare but potentially life-threatening conditions resulting from concomitant administration of serotonergic drugs (including Serotonin Reuptake Inhibitors, Serotonin and Norepinephrine Reuptake Inhibitors and tricyclic antidepressants) *[see Warnings and Precautions (5.8)]*.

Patients should be advised to inform their physicians if they are taking, or plan to take, any prescription or over-the-counter drugs as there is a potential for interactions *[see Drug Interactions (7)]*.

17.9 Alcohol

Patients should be advised to avoid alcohol while taking TRADENAME™ *[see Drug Interactions (7.3)]*.

7.10 Medication Guide

See Medication Guide.

Manufactured by:
Janssen Ortho, LLC
Gurabo, PR 00778

Manufactured for:
PriCara, Division of Ortho-McNeil-Janssen Pharmaceuticals, Inc.
Raritan, NJ 08869

PriCara®

Division of Ortho-McNeil-Janssen
Pharmaceuticals, Inc.

ORTHO-McNEIL-JANSSEN™

PHARMACEUTICALS, INC.

MEDICATION GUIDE
TRADENAME™
(tapentadol)
immediate release oral tablets

- **Keep TRADENAME™ in a safe place to prevent theft. Selling or giving away TRADENAME™ may harm others, and is against the law.**
- **Tell your doctor if you (or a family member) have ever abused or been dependent on alcohol, prescription medicines, or street drugs.**

Read the Medication Guide that comes with TRADENAME™ before you start taking it and each time you get a new prescription. There may be new information. This Medication Guide does not take the place of talking to your doctor about your medical condition or your treatment. Talk to your doctor if you have any questions.

What is the most important information I should know about TRADENAME™?

TRADENAME™ is a tablet that contains tapentadol, a strong medicine that is a pain medicine.

Use TRADENAME™ exactly how your doctor tells you to. Do not use TRADENAME™ if it has not been prescribed for you.

You should not take TRADENAME™ if your pain is mild and can be controlled with other pain medicines such as non-steroidal anti-inflammatory medicines (NSAIDS) or acetaminophen.

What is TRADENAME™?

- TRADENAME™ is a prescription medicine that is used in adults 18 years of age or older to treat moderate to severe pain that is expected to last a short time.

  TRADENAME™ is for short-term use only because the risks for withdrawal symptoms, abuse and addiction are higher when TRADENAME™ is used longer.

Who should not take TRADENAME™?
Do not take TRADENAME™ if you:

- have severe lung problems
- have a gastrointestinal problem called paralytic ileus in which the intestines are not working normally.
- take a monoamine oxidase inhibitor (MAOI) medicine or have taken an MAOI within the last 14 days. Ask your doctor or pharmacist if any of your medicines is an MAOI.

What should I tell my doctor before taking TRADENAME™?

TRADENAME™ may not be right for you. Tell your doctor about all your medical conditions, including if you have:

- trouble breathing or lung problems
- or had a head injury
- liver or kidney problems
- convulsions or seizures
- dependency problems with alcohol
- pancreas or gall bladder problems
- past or present substance abuse or drug addiction. There is a risk of abuse or addiction with narcotic pain medicines. If you have abused drugs in the past, you may have a higher chance of developing abuse or addiction again while using TRADENAME™.
- are pregnant or plan to become pregnant
- are breast-feeding. You should not breast-feed while taking TRADENAME™.

Tell your doctor about all the medicines you take, including prescription and nonprescription medicines, vitamins, and herbal supplements. Using TRADENAME™ with other medicines can cause serious side effects. The doses of some other medicines may need to be changed. Your doctor can tell you what medicines can be safely taken with TRADENAME™. Especially tell your doctor if you take:

- **Monoamine Oxidase Inhibitors (MAOIs).** See "Who should not take TRADENAME™."
- **any medicine that makes you sleepy.** TRADENAME™ can make you sleepy and affect your breathing. Taking these medicines together can be dangerous.

How should I take TRADENAME™?

- Do not take TRADENAME™ unless it has been prescribed for you by your doctor.
- Take TRADENAME™ exactly as prescribed by your doctor.
- **Do not change the dose of TRADENAME™ unless your doctor tells you to.** Your doctor may change your dose after seeing how the medicine affects you. Do not use TRADENAME™ more often than prescribed. Call your doctor if your pain is not well controlled while taking TRADENAME™.
- Follow your doctor's instructions about how to slowly stop taking TRADENAME™ to help lessen withdrawal symptoms.
- TRADENAME™ can be taken with or without food.

What should I avoid while taking TRADENAME™?

- Do not drive, operate machinery, or participate in any other possibly dangerous activities until you know how you react to this medicine. TRADENAME™ can make you sleepy.
- You should not drink alcohol while using TRADENAME™. Alcohol increases your chance of having dangerous side effects.

What are the possible side effects of TRADENAME™?

TRADENAME™ can cause serious side effects including:

- **Life-threatening breathing problems. Call your doctor right away or get emergency medical help if you:**
  - have trouble breathing, or have slow or shallow breathing
  - have a slow heartbeat
  - have severe sleepiness
  - have cold, clammy skin
  - feel faint, dizzy, confused, or can not think, walk or talk normally
  - have a seizure
  - have hallucinations
- **Physical Dependence.** TRADENAME™ can cause physical dependence. Talk to your doctor about slowly stopping TRADENAME™ to avoid getting sick with withdrawal symptoms. You could become sick with uncomfortable symptoms because your body has become used to the medicine. Tell your doctor if you have any of these symptoms of withdrawal: feeling anxious, sweating, sleep problems, shivering, pain, nausea, tremors, diarrhea, upper respiratory symptoms, hallucinations, hair "standing on end." Physical dependence is not the same as drug addiction. Your doctor can tell you more about the differences between physical dependence and drug addiction.
- **Serotonin syndrome.** Serotonin syndrome is a rare, life-threatening problem that could happen if you take TRADENAME™ with Selective Serotonin Reuptake Inhibitors (SSRIs), Serotonin and Norepinephrine Reuptake Inhibitors (SNRIs), Monoamine Oxidase Inhibitors (MAOIs), triptans or certain other medicines. Call your doctor or get medical help right away if you have any one or more of the these symptoms: you feel agitated, have hallucinations, coma, rapid heart beat, feel overheated, loss of coordination, over active reflexes, nausea, vomiting, or diarrhea.
- **Seizures.** TRADENAME™ can cause seizures in people who are at risk for seizures or who

have epilepsy. Tell your doctor right away if you have a seizure and stop taking TRADENAME™.

- **Low blood pressure.** This can make you feel dizzy if you get up too fast from sitting or lying down.

The common side effects with TRADENAME™ are nausea, dizziness, vomiting, sleepiness, and itching.

Constipation is a common side effect of all opioid medicines. Talk to your doctor about the use of laxatives and stool softeners to prevent or treat constipation while taking TRADENAME™.

Tell your doctor about any side effect that bothers you or that does not go away. These are not all the possible side effects of TRADENAME™. For a complete list, ask your doctor or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store TRADENAME™?

- Store TRADENAME™ at 59°F to 86°F (15°C to 30°C). Keep TRADENAME™ tablets dry.
- Dispose of TRADENAME™ tablets you no longer need.

Keep TRADENAME™ in a safe place out of the reach of children.

General information about TRADENAME™

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use TRADENAME™ for a condition for which it was not prescribed. **Do not give TRADENAME™ to other people, even if they have the same symptoms you have. Sharing TRADENAME™ could be harmful and is against the law.**

This Medication Guide summarizes the most important information about TRADENAME™. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about TRADENAME™ that is written for doctors. For more information about TRADENAME™ call 1-800-526-7736.

What are the ingredients in TRADENAME™?

Active Ingredient: tapentadol
Inactive ingredients: microcrystalline cellulose, lactose monohydrate, croscarmellose sodium, povidone, magnesium stearate, and Opadry® II, a proprietary film-coating mixture containing polyvinyl alcohol, titanium dioxide, polyethylene glycol, talc, and aluminum lake coloring.

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

Issued November 2008

Manufactured by:
Janssen Ortho, LLC
Gurabo, PR 00778

Manufactured for:
PriCara, Division of Ortho-McNeil-Janssen Pharmaceuticals, Inc.
Raritan, NJ 08869