**Material Safety Data Sheet**
# Tramadol Hydrochloride and Acetaminophen Tablets

**Strength:** 37.5 mg/325 mg per Tablet **Pack Size:** 100/500/1000 Tablet Per bottle **Revision No.:** 00

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**EMERGENCY OVERVIEW**

Each tramadol hydrochloride and acetaminophen tablets intended for oral administration contains tramadol hydrochloride, 37.5 mg and acetaminophen, 325 mg and excipients generally considered to be non- toxic and non-hazardous in small quantities and under conditions of normal occupational exposure.

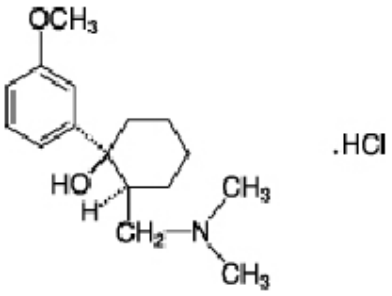
## Section 1. Identification of the substance

**Identification of the product**

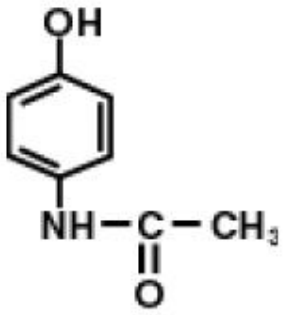
**Product name:** Tramadol Hydrochloride and Acetaminophen Tablets

**Chemical Name:** (±)*cis*-2-[(dimethylamino)methyl]-1-(3-methoxyphenyl) cyclohexanol hydrochloride. (Tramadol hydrochloride)/ *N*-acetyl-*p*-aminophenol (Acetaminophen)

**Therapeutic Category** Analgesics




Tramadol Hydrochloride




Acetaminophen

**Manufacturer / supplier identification**

| | |
|---|---|
| **Company:** | **Cadila Healthcare Ltd. Ahmedabad, India** |
| **Contact for information:** | Tel.: +91 79 6868100 Fax: +91 79 3750319 |
| **Emergency telephone No.** | Tel.: +91 79 6868100 |

## Section 2. Composition / information on ingredients

| Component | Exposure Limit | CAS No. |
|---|---|---|
| **Principle Component :** | | |
| Tramadol hydrochloride | Not Found | 36282-47-0 |
| Acetaminophen | Not Found | 103-90-2 |
| **Inactive Ingredients :** | | |
| corn starch | Not Found | 9005-25-8 |
| hypromellose | Not Found | 9004-65-3 |
| magnesium stearate | Not Found | 577-04-0 |
| microcrystalline cellulose | Not Found | 9004-34-6 |
| polyethylene glycol | Not Found | 57-55-6 |

| | | |
|---|---|---|
| pregelatinized starch | Not Found | 9005-25-8 |
| sodium starch glycolate | Not Found | 9063-38-1 |
| talc | Not Found | 14807-96-6 |
| titanium dioxide. | Not Found | 13463-67-7 |

## Section 3. Health Hazards Information

Dose and Administration

For the short-term (five days or less) management of acute pain, the recommended dose of tramadol hydrochloride and acetaminophen tablets is 2 tablets every 4 to 6 hours as needed for pain relief up to a maximum of 8 tablets per day.

**Individualization of Dose:**
In patients with creatinine clearances of less than 30 mL/min, it is recommended that the dosing interval of tramadol hydrochloride and acetaminophen tablets be increased not to exceed 2 tablets every 12 hours. Dose selection for an elderly patient should be cautious, in view of the potential for greater sensitivity to adverse events.

Adverse Effects

**Incidence of Treatment-Emergent Adverse Events (≥2.0%)**
**Gastrointestinal System Disorders:** Constipation, Diarrhea, Nausea, Dry Mouth
**Psychiatric Disorders:** Somnolence, Anorexia, Insomnia
**Central & Peripheral Nervous System:** Dizziness
**Skin and Appendages** :Sweating Increased, Pruritus
**Reproductive Disorders:** Prostatic Disorder
**Incidence at least 1%, causal relationship at least possible or greater:**
***Body as a Whole:*** Asthenia, fatigue, hot flushes
***Central and Peripheral Nervous System:*** Dizziness, headache, tremor
***Gastrointestinal System:*** Abdominal pain, constipation, diarrhea, dyspepsia, flatulence, dry mouth, nausea, vomiting
***Psychiatric Disorders:*** Anorexia, anxiety, confusion, euphoria, insomnia, nervousness, somnolence
***Skin and Appendages:***Pruritus, rash, increased sweating.
**Selected Adverse events occurring at less than 1%*:***
***Body as a Whole:*** Chest pain, rigors, syncope, withdrawal syndrome
***Cardiovascular Disorders:*** Hypertension, aggravated hypertension, hypotension
***Central and Peripheral Nervous System:*** Ataxia, convulsions, hypertonia, migraine, aggravated migraine, involuntary muscle contractions, paresthesias, stupor, vertigo
***Gastrointestinal System:*** Dysphagia, melena, tongue edema
***Hearing and Vestibular Disorders:*** Tinnitus

***Heart Rate and Rhythm Disorders:*** Arrhythmia, palpitation, tachycardia
***Liver and Biliary System:***Hepatic function abnormal
***Metabolic and Nutritional Disorders:*** Weight decrease
***Psychiatric Disorders:***Amnesia, depersonalization, depression, drug abuse, emotional lability, hallucination, impotence, paroniria, abnormal thinking
***Red Blood Cell Disorders:*** Anemia
***Respiratory System:*** Dyspnea
***Urinary System:*** Albuminuria, micturition disorder, oliguria, urinary retention
***Vision Disorders:*** Abnormal vision

**Other clinically significant adverse experiences previously reported with tramadol hydrochloride:**

Other events which have been reported with the use of tramadol products and for which a causal association has not been determined include: vasodilation, orthostatic hypotension, myocardial ischemia, pulmonary edema, allergic reactions (including anaphylaxis and urticaria, Stevens-Johnson syndrome/TENS), cognitive dysfunction, difficulty concentrating, depression, suicidal tendency, hepatitis liver failure and gastrointestinal bleeding. Reported laboratory abnormalities included elevated creatinine and liver function tests. Serotonin syndrome (whose symptoms may include mental status change, hyperreflexia, fever, shivering, tremor, agitation, diaphoresis, seizures and coma) has been reported with tramadol when used concomitantly with other serotonergic agents such as SSRIs and MAOIs.

**Other clinically significant adverse experiences previously reported with acetaminophen:**

Allergic reactions (primarily skin rash) or reports of hypersensitivity secondary to acetaminophen are rare and generally controlled by discontinuation of the drug and, when necessary, symptomatic treatment.

Over Dose Effect

The initial symptoms seen within the first 24 hours following an acetaminophen overdose are: anorexia, nausea, vomiting, malaise, pallor and diaphoresis.

Acute over dosage with tramadol can be manifested by respiratory depression, somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, constricted pupils, seizures, bradycardia, hypotension, cardiac arrest, and death.

Medical Conditions

- Patients should be informed that tramadol hydrochloride and acetaminophen tablets may cause seizures and/or serotonin syndrome with concomitant use of serotonergic agents (including SSRIs, SNRIs, and triptans) or drugs that significantly reduce the metabolic clearance of tramadol.
- Tramadol hydrochloride and acetaminophen tablets may impair mental or physical abilities required for the performance of

potentially hazardous tasks such as driving a car or operating machinery.

- Tramadol hydrochloride and acetaminophen tablets should not be taken with alcohol containing beverages.
- The patient should be instructed not to take tramadol hydrochloride and acetaminophen tablets in combination with other tramadol or acetaminophen-containing products, including over-the-counter preparations.
- Tramadol hydrochloride and acetaminophen tablets should be used with caution when taking medications such as tranquilizers, hypnotics or other opiate containing analgesics.
- The patient should be instructed to inform the physician if they are pregnant, think they might become pregnant, or are trying to become pregnant
- The patient should understand the single-dose and 24-hour dose limit and the time interval between doses, since exceeding these recommendations can result in respiratory depression, seizures, hepatic toxicity and death.

Contraindications

Tramadol hydrochloride and acetaminophen tablets should not be administered to patients who have previously demonstrated hypersensitivity to tramadol, acetaminophen, any other component of this product or opioids. Tramadol hydrochloride and acetaminophen tablets are contraindicated in any situation where opioids are contraindicated, including acute intoxication with any of the following: alcohol, hypnotics, narcotics, centrally acting analgesics, opioids or psychotropic drugs. Tramadol hydrochloride and acetaminophen tablets may worsen central nervous system and respiratory depression in these patients.

Pregnancy Comments

There are no adequate and well-controlled studies in pregnant women. Tramadol hydrochloride and acetaminophen tablets should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Neonatal seizures, neonatal withdrawal syndrome, fetal death and still birth have been reported with tramadol hydrochloride during post-marketing.

**Labor and Delivery:**

Tramadol hydrochloride and acetaminophen tablets should not be used in pregnant women prior to or during labor unless the potential benefits outweigh the risks. Safe use in pregnancy has not been established. Chronic use during pregnancy may lead to physical dependence and post-partum withdrawal symptoms in the newborn . Tramadol has been shown to cross the placenta. The mean ratio of serum tramadol in the umbilical veins compared to maternal veins was 0.83 for 40 women given tramadol during labor.

**Nursing Mothers:**

Tramadol hydrochloride and acetaminophen tablets are not recommended for obstetrical preoperative medication or for post-delivery analgesia in nursing mothers because its safety in infants and newborns has not been

studied.

Pregnancy Category *Category C*

## Section 4. First aid measures

Overdose Treatment In the treatment of tramadol overdosage, primary attention should be given to the re-establishment of a patent airway and institution of assisted or controlled ventilation. 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.
Standard recommendations should be followed for the treatment of acetaminophen overdose.

## Section 5. Fire – fighting measures

| | | | |
|---|---|---|---|
| **Flash point** | Not Found | **Upper Flammable Limit:** | Not Found |
| **Auto-Ignition Temperature:** | Not Found | **Lower Flammable Limit:** | Not Found |
| **Extinguishing Media** | Water Spray, dry chemical, carbon dioxide or foam as appropriate for surrounding fire and material. | **Fire and Explosion Hazard** | This material is assumed to be combustible.<br>As with all dry powders it is advisable to ground mechanical equipment in contact with the dry material to dissipate the potential build up of static electricity. |

**Fire Fighting Procedure** As with all fires, evacuate personnel to a safe area. Fire fighter should use self- contained breathing equipment and protective clothing.

## Section 6. Accidental Release Measures

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| Spill Response | Wear approved respiratory protection, chemically compatible gloves and protective clothing. Wipe up spillage or collect spillage using high efficiency vacuum cleaner. Avoid breathing dust. Place spillage in appropriately labelled container for disposal. Wash spill site. |

## Section 7. Handling and Storage

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|---|---|
| Storage | Store at 20° to 25°C (68° to 77°F)<br><br>Dispense in a tight container. |

## Section 8. Exposure controls and personal protection

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|---|---|
| Respiratory Protection | Protection from inhalation is not normally necessary. If ventilation is inadequate or dust is likely to generate, use of suitable dust mask would be appropriate. |
| Skin Protection | Skin protection is not normally necessary, however it is good practice to avoid contact with chemical to use suitable gloves when handling. |
| Eye protection | Eye protection is not normally necessary. If concerned wear protective goggles or glasses. Wash hands prior to touching eye and in particular handling contact lenses. |
| Protective Clothing | Protective clothing is not normally necessary, however it is good practice to use apron. |

## Section 9. Physical and chemical properties

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|---|---|---|---|
| **Appearance** | Tramadol Hydrochloride and Acetaminophen Tablets, 37.5 mg/325 mg are white-color, capsule-shaped, bevel, biconvex, film-coated tablet, debossing "334" on one side and plain on other side | | |
| **Solubility in water** | No Data Available | **Odour** | Odourless |
| **Boiling point** | No Data Available | **Melting Point** | No Data Available |
| **Evaporation rate** | No Data Available | **Vapour density** | No Data Available |
| **Reactivity in water** | No Data Available | **Evaporation rate** | No Data Available |
| **Percentage Volatile by volume** | No Data Available | **Specific gravity** | No Data Available |

| | |
|---|---|
| **Vapour pressure** | No Data Available |
| **Other information** | Not Applicable |

## Section 10. Stability and Reactivity

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|---|---|---|---|
| **Condition to avoid** | Avoid exposure to extreme heat, light and moisture. | **Stable** | Stable under normal ambient and anticipated storage and handling conditions. |
| **Decomposition Products** | No Data Available | **Hazardous Reaction** | No data available. |
| **Incompatibilities** | No data available. | | |

## Section 11. Toxicological information

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|---|---|
| General | Handling of formulated product is not expected to cause any toxicological affects. The data pertains to the ingredient in formulations, rather than this specie formulation. |
| Target organ | Eye contact, Skin contact and inhalation is not great risk as this product is tablet. |
| other | Not Applicable |

## Section 12. Ecological information

Do not allow product to enter drinking water supplies, waste water or soil

## Section 13. Disposal Consideration

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|---|---|
| **Disposal** | Dispose the waste in accordance with all applicable Federal, State and local laws. |

## Section 14. Transport Information

May be shipped normally as a non hazardous material.

## Section 15. Regulatory Information

ANDA no.- 90460

## Section 16. Other information

None

**Date of issue:** 19/05/2012 **Supersedes edition of:** New Edition

The information contained herein is based on the state of our knowledge. It Characterises the product with regard to the appropriate safety precautions. It does not represent a guarantee of the properties of the product.