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

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 structure](image-url)
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![Acetaminophen](image)  

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  

<table>
<thead>
<tr>
<th>Component</th>
<th>Exposure Limit</th>
<th>CAS No.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Principle Component:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tramadol hydrochloride</td>
<td>Not Found</td>
<td>36282-47-0</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>Not Found</td>
<td>103-90-2</td>
</tr>
<tr>
<td><strong>Inactive Ingredients:</strong></td>
<td></td>
<td></td>
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<tr>
<td>corn starch</td>
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<td>9005-25-8</td>
</tr>
<tr>
<td>hypromellose</td>
<td>Not Found</td>
<td>9004-65-3</td>
</tr>
<tr>
<td>magnesium stearate</td>
<td>Not Found</td>
<td>577-04-0</td>
</tr>
<tr>
<td>microcrystalline cellulose</td>
<td>Not Found</td>
<td>9004-34-6</td>
</tr>
<tr>
<td>polyethylene glycol</td>
<td>Not Found</td>
<td>57-55-6</td>
</tr>
</tbody>
</table>
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
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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

<table>
<thead>
<tr>
<th>Flash point</th>
<th>Not Found</th>
<th>Upper Flammable Limit:</th>
<th>Not Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>Auto-Ignition Temperature:</td>
<td>Not Found</td>
<td>Lower Flammable Limit:</td>
<td>Not Found</td>
</tr>
<tr>
<td>Extinguishing Media</td>
<td>Water Spray, dry chemical, carbon dioxide or foam as appropriate for surrounding fire and material.</td>
<td>Fire and Explosion Hazard</td>
<td>This material is assumed to be combustible. 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.</td>
</tr>
<tr>
<td>Fire Fighting Procedure</td>
<td>As with all fires, evacuate personnel to a safe area. Fire fighter should use self- contained breathing equipment and protective clothing.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Section 6.  Accidental Release Measures
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

Storage

Store at 20° to 25°C (68° to 77°F)
Dispense in a tight container.

Section 8. Exposure controls and personal protection

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

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
Section 10. Stability and Reactivity

**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

**General**
Handling of formulated product is not expected to cause any toxicological affects. The data pertains to the ingredient in formulations, rather than this species 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

**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

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.