SAFETY DATA SHEETS

This SDS packet was issued with item:

078948605

The safety data sheets (SDS) in this packet apply to the individual products listed below. Please refer to invoice for specific item number(s).

078948567 078948609 078950202 078950204 078950205

Safety Data Sheet

SECTION 1. IDENTIFICATION

Common/Trade Name: Amitriptyline Hydrochloride Tablets USP

Chemical Name: 10,11-Dihydro-N,N-dimethyl-5H-dibenzo[a, d] cycloheptene-Δ5 , γ-propylamine hydrochloride

Synonyms: Not Available

Molecular Formula: $C_{20}H_{23}N.HCl$

Molecular Weight: 313.90

CAS No: 549-18-8

Product Group: Antidepressant

Manufacturer's Name	Unichem Laboratories Limited
Address	Unichem Laboratories Limited, Pilerne, Bardez, Goa, India.
Marketed by	Unichem Pharmaceuticals (USA), Inc. 1 Tower Center Blvd., Suite 2200 East Brunswick, NJ 08816
Phone Number	(732) 253 5954 (Fax : (732) 325 0572)
Emergency Phone No.	1-866-562-4616

Recommended Use: Amitriptyline Hydrochloride is indicated for the relief of symptoms of depression. Endogenous depression is more likely to be alleviated than are other depressive states.

Restriction on Use: Prescription Only.

SECTION 2. HAZARD(s) IDENTIFICATION

Emergency Overview

Physical State:

10 mg: Pink colored, round shaped, film-coated tablets, debossed with "60" on one side and "U" on the other side.

25 mg: Yellow colored, round shaped, film-coated tablets, debossed with "420" on one side and "U" on the other side

50 mg: Brown colored, round shaped, film-coated tablets, debossed with "421" on one side and "U" on the other side

75 mg: Yellow colored, round shaped, film-coated tablets, debossed with "422" on one side and "U" on the other side

100 mg: Orange colored, round shaped, film-coated tablets, debossed with "423" on one side and "U" on the other side

150 mg: Green colored, Capsule shaped, film-coated tablets, debossed with "424" on one side and "U" on the other side

Odor: No Data Available

WARNING:

- **Clinical Worsening and Suicide Risk:** Patients with major depressive disorder (MDD), both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality) or unusual changes in behavior, whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs. Suicide is a known risk of depression and certain other psychiatric disorders, and these disorders themselves are the strongest predictors of suicide. There has been a long-standing concern, however, that antidepressants may have a role in inducing worsening of depression and the

emergence of suicidality in certain patients during the early phases of treatment.

All patients being treated with antidepressants for any indication should be monitored appropriately and observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases.

The following symptoms, anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, and mania, have been reported in adult and pediatric patients being treated with antidepressants for major depressive disorder as well as for other indications, both psychiatric and nonpsychiatric. Although a causal link between the emergence of such symptoms and either the worsening of depression and/or the emergence of suicidal impulses has not been established, there is concern that such symptoms may represent precursors to emerging suicidality.

Consideration should be given to changing the therapeutic regimen, including possibly discontinuing the medication, in patients whose depression is persistently worse, or who are experiencing emergent suicidality or symptoms that might be precursors to worsening depression or suicidality, especially if these symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms.

Families and caregivers of patients being treated with antidepressants for major depressive disorder or other indications, both psychiatric and nonpsychiatric, should be alerted about the need to monitor patients for the emergence of agitation, irritability, unusual changes in behavior, and the other symptoms described above, as well as the emergence of suicidality, and to report such symptoms immediately to health care providers. Such monitoring should include daily observation by families and caregivers.

Prescriptions for amitriptyline hydrochloride tablets should be written for the smallest quantity of tablets consistent with good patient management, in order to reduce the risk of overdose

- **Screening Patients for Bipolar Disorder:** A major depressive episode may be the initial presentation of bipolar disorder. It is generally believed (though not established in controlled trials) that treating such an episode with an antidepressant alone may increase the likelihood of precipitation of a mixed/manic episode in patients at risk for bipolar disorder. Whether any of the symptoms described above represent such a conversion is unknown. However, prior to initiating treatment with an antidepressant, patients with depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression. It should be noted that amitriptyline hydrochloride is not approved for use in treating bipolar depression.

Amitriptyline hydrochloride may block the antihypertensive action of guanethidine or similarly acting compounds.

It should be used with caution in patients with a history of seizures and, because of its atropine-like action, in patients with a history of urinary retention or angle-closure glaucoma. In patients with angle closure glaucoma, even average doses may precipitate an attack.

Patients with cardiovascular disorders should be watched closely. Tricyclic antidepressant drugs, including amitriptyline hydrochloride, particularly when given in high doses, have been reported to produce arrhythmias, sinus tachycardia, and prolongation of the conduction time. Myocardial infarction and stroke have been reported with drugs of this class.

Close supervision is required when amitriptyline hydrochloride is given to hyperthyroid patients or those receiving thyroid medication.

Amitriptyline hydrochloride may enhance the response to alcohol and the effects of barbiturates and other CNS depressants. In patients who may use alcohol excessively, it should be borne in mind that the potentiation may increase the danger inherent in any suicide attempt or overdosage. Delirium has been reported with concurrent

<table>
<tr><td></td><td colspan="2">administration of amitriptyline and disulfiram.
• Angle-Closure Glaucoma: The pupillary dilation that occurs following use of many antidepressant drugs including amitriptyline hydrochloride may trigger an angle closure attack in a patient with anatomically narrow angles who does not have a patent iridectomy.
• Usage in Pregnancy: Teratogenic effects were not observed in mice, rats, or rabbits when amitriptyline was given orally at doses of 2 to 40 mg/kg/day (up to 13 times the maximum recommended human dose[1]). Studies in literature have shown amitriptyline to be teratogenic in mice and hamsters when given by various routes of administration at doses of 28 to 100 mg/kg/day (9 to 33 times the maximum recommended human dose), producing multiple malformations. Another study in the rat reported that an oral dose of 25 mg/kg/day (8 times the maximum recommended human dose) produced delays in ossification of fetal vertebral bodies without other signs of embryotoxicity. In rabbits, an oral dose of 60 mg/kg/day (20 times the maximum recommended human dose) was reported to cause incomplete ossification of cranial bones.
Amitriptyline has been shown to cross the placenta. Although a causal relationship has not been established, there have been a few reports of adverse events, including CNS effects, limb deformities, or developmental delay, in infants whose mothers had taken amitriptyline during pregnancy.
There are no adequate and well-controlled studies in pregnant women. Amitriptyline hydrochloride should be used during pregnancy only if the potential benefit to the mother justifies the potential risk to the fetus.
[1]Based on a maximum recommended amitriptyline dose of 150 mg/day or 3 mg/kg/day for a 50 kg patient.
• Nursing Mothers: Amitriptyline is excreted into breast milk. In one report in which a patient received amitriptyline 100 mg/day while nursing her infant, levels of 83 to 141 ng/mL were detected in the mother's serum. Levels of 135 to 151 ng/mL were found in the breast milk, but no trace of the drug could be detected in the infant's serum.
Because of the potential for serious adverse reactions in nursing infants from amitriptyline, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.
• Usage in Pediatric Patients: In view of the lack of experience with the use of this drug in pediatric patients, it is not recommended at the present time for patients under 12 years of age.</td></tr>
<tr><td>Primary Route(s) of Entry</td><td colspan="2">Ingestion</td></tr>
<tr><td rowspan="4">Potential Health Effects:</td><td>Eyes</td><td>Not expected to be hazard to eyes in final pharmaceutical form.</td></tr>
<tr><td>Skin</td><td>May cause an allergic skin reaction.</td></tr>
<tr><td>Inhalation</td><td>Not expected to be an inhalation hazard in the final pharmaceutical form</td></tr>
<tr><td colspan="2">Please see Patient Package Insert for further information</td></tr>
<tr><td>Toxicity Data:</td><td colspan="2">See Section 11</td></tr>
<tr><td>Effects of Over Exposure:</td><td colspan="2">Deaths may occur from overdosage with this class of drugs. Multiple drug ingestion (including alcohol) is common in deliberate tricyclic antidepressant overdose. As the management is complex and changing, it is recommended that the physician contact a poison control center for current information on treatment. Signs and symptoms of toxicity develop rapidly after tricyclic antidepressant overdose, therefore, hospital monitoring is required as soon as possible.
Critical manifestations of overdose include: cardiac dysrhythmias, severe hypotension, convulsions, and CNS depression, including coma. Changes in the electrocardiogram particularly in QRS axis or width, are clinically significant indicators of tricyclic antidepressant toxicity. In addition, a rightward axis shift in the terminal QRS complex together with a prolonged QT interval and sinus tachycardia are specific and sensitive indicators of first generation tricyclic overdose. The absence of these findings is not exclusionary. Prolonged PR interval, ST-T wave changes, ventricular tachycardia and</td></tr>
</table>

	fibrillation may also occur. Other signs of overdose may include: impaired myocardial contractility, confusion, disturbed concentration, transient visual hallucinations, dilated pupils, disorders of ocular motility, agitation, hyperactive reflexes polyradiculoneuropathy, stupor, drowsiness, muscle rigidity, vomiting, hypothermia, hyperpyrexia, or any of the symptoms listed under ADVERSE REACTIONS section of Patient Package Insert.	
SECTION 3. COMPOSITION / INFORMATION ON INGREDIENTS		
Composition	**CAS #**	**Quantity**
Amitriptyline Hydrochloride (active ingredient)	549-18-8	10 mg, 25 mg, 50 mg, 75 mg, 100 mg and 150 mg
REFER to PHYSICIAN'S DESK REFERENCE for common components		
Target Organs:	Brain	
SECTION 4. FIRST-AID MEASURES		
Eye Contact	Rinse cautiously with water. Remove contact lenses, if present and easy to do. Continue rinsing. Obtain medical attention.	
Skin Contact	Remove contaminated clothing. Wash off with soap and plenty of water. Obtain medical attention if irritation develops or persists.	
Ingestion	Do not induce vomiting. Rinse mouth. Immediately call a POISON CENTER or doctor/physician.	
Inhalation	Move to fresh air. Call a physician if symptoms develop or persist.	
Most important symptoms/effects, acute and delayed	For information on potential signs and symptoms of exposure, See Section 2 - Hazards Identification and/or Section 11 - Toxicological Information.	
Indication of immediate medical attention and special treatment needed	If you feel unwell, seek medical advice (show the label where possible)	
General information	The recommendations in this section are intended for manufacturing or other situations where exposure to contents may occur.	
SECTION 5. FIRE-FIGHTING MEASURES		
Flammability	No data available	
Flash Point	No data available	
Extinguishing Media	Use fire-extinguishing media appropriate for surrounding materials. Water. Foam. Dry chemical or CO_2.	
Special Fire Fighting Procedures	During all fire fighting activities, wear appropriate protective equipment, including self contained breathing apparatus.	
Unusual Fire/Explosion Hazards	Not applicable	
Hazardous Combustion Products	No data available	
SECTION 6. ACCIDENTAL RELEASE MEASURES		
STEPS TO BE TAKEN IF SIGNIFICANT QUANTITIES ARE SPILLED: Keep unnecessary personnel away. Do not touch damaged containers or spilled material unless wearing appropriate protective clothing. Ensure adequate ventilation. Avoid inhalation of dust from the spilled material. Wear appropriate personal protective equipment. Sweep up or vacuum up spillage and collect in suitable container for disposal. Avoid the generation of dusts during clean-up. Clean surface thoroughly to remove residual contamination.		
SECTION 7. HANDLING AND STORAGE		
Precautions **General Handling:**	If tablets are broken/crushed, avoid breathing dust and avoid contact with eyes, skin, and clothing. When handling, use appropriate personal protective equipment (see Section 8).	
Storage	Store at 20º to 25ºC (68º to 77ºF); excursions permitted to 15° to 30°C (59° to 86°F) [See USP Controlled Room Temperature], in a tight, light resistant container.	

SECTION 8. EXPOSURE CONTROLS / PERSONAL PROTECTION		
Engineering Controls	Airborne exposure should be controlled primarily by engineering controls such as general dilution ventilation, local exhaust ventilation, or process enclosure.	
Respiratory Protection	Where respirators are deemed necessary to reduce or control occupational exposures, use NIOSH-approved respiratory protection and have an effective respirator program in place.	
Personal Protection	**Eye/face Protection**	Safety glasses with side shields recommended. If splash potential or dusty operations, wear goggles/face shield.
	Skin Protection	Chemical resistant gloves.
	General Hygiene Considerations	Engineering controls should be used as the primary means to control workplace exposures. Follow good workplace hygiene practices such as washing hands after handling this material.
	Other	Chemical-resistant gloves and impermeable body covering to minimize skin contact.
Recommended Facilities	Eye wash, washing facilities	

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES					
Appearance	Solid – film coated tablets	Melting point	198 -200°C	Solubility in water	freely soluble in water and alcohol
Odor	N/A	Boiling point	N/A	Specific Gravity	N/A
Taste	N/A	Vapor Pressure	N/A	Flashpoint	N/A
pH	N/A	Density	N/A	Flammability Limits	N/A

SECTION 10. STABILITY AND REACTIVITY	
Stability	Stable under recommended handling and storage conditions (see section 7).
Incompatibility	Strong oxidizing agents
Hazardous Decomposition	Formation of toxic gases is possible during heating or in case of fire.
Conditions to Avoid	Heat
Hazardous Polymerization	Data not available

SECTION 11. TOXICOLOGICAL INFORMATION

Oral toxicity (LD50): 240 mg/kg [Rat]

Maximum Daily Dose (MDD), Oral

Amitriptyline Hydrochloride: 300 mg

Carcinogenicity, Mutagenesis, Impairment of Fertility: Data not available.

Teratogenicity: Teratogenic effects were not observed in mice, rats, or rabbits when amitriptyline was given orally at doses of 2 to 40 mg/kg/day (up to 13 times the maximum recommended human dose[1]). Studies in literature have shown amitriptyline to be teratogenic in mice and hamsters when given by various routes of administration at doses of 28 to 100 mg/kg/day (9 to 33 times the maximum recommended human dose), producing multiple malformations. Another study in the rat reported that an oral dose of 25 mg/kg/day (8 times the maximum recommended human dose) produced delays in ossification of fetal vertebral bodies without other signs of embryotoxicity. In rabbits, an oral dose of 60 mg/kg/day (20 times the maximum recommended human dose) was reported to cause incomplete ossification of cranial bones.

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There are no adequate and well-controlled studies in pregnant women. Amitriptyline hydrochloride should be used during pregnancy only if the potential benefit to the mother justifies the potential risk to the fetus.

[1] Based on a maximum recommended amitriptyline dose of 150 mg/day or 3 mg/kg/day for a 50 kg patient.

SECTION 12. ECOLOGICAL INFORMATION

Slightly hazardous for water. Do not allow undiluted product to reach ground water, water course or sewage system
Avoid release to the environment.

SECTION 13. DISPOSAL CONSIDERATIONS

Waste Disposal Method Dispose of contents and container according to local, regional, national, and international regulations

SECTION 14. TRANSPORT INFORMATION
The Material Safety Data Sheet (MSDS) should accompany all shipments for reference in the event of spillage or accidental release. Transportation and shipping of this product is not restricted. It has no known significant hazards requiring special packaging or labeling for air, maritime or ground transport purpose.
SECTION 15. REGULATORY INFORMATION
US FDA: Amitriptyline Hydrochloride Tablets USP are an approved prescription medication in USA.
SECTION 16. OTHER INFORMATION
ABBEVIATIONS: CNS: Central Nervous System USP: United States Pharmacopoeia US FDA: United States Food & Drug Administration
Prepared by: Unichem Laboratories Limited
References: 1. Amitriptyline Hydrochloride Safety data sheet (SDS# VPCL/SDS/006/00) by Vasudha Pharma Chem Limited., India. 2. British Pharmacopoeia – Safety Data Sheet (Version no. 2), Revision: 07.06.2013 3. Amitriptyline Hydrochloride Tablets USP, Package Insert, Unichem Laboratories Limited, India.
Date: May 25, 2021 - Version: 000
SEE CURRENT PACKAGE INSERT FOR FURTHER INFORMATION