Safety Data Sheet

Duloxetine delayed-release capsules USP

Strength: 20 mg, 30 mg, 60mg **Pack Size:** 30/60/90 capsules per bottle for 20 mg
30/90 capsules per bottle for 30 mg and 60 mg. **Revision No.:** 02

EMERGENCY OVERVIEW

Each Duloxetine delayed-release capsules intended for oral administration contains Duloxetine hydrochloride and excipients generally considered to be non- toxic and non-hazardous in small quantities and under conditions of normal occupational exposure.

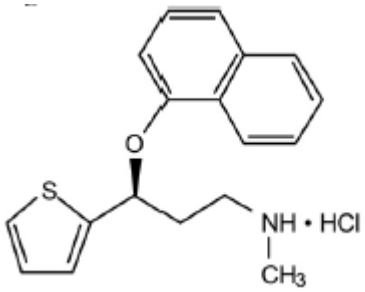
Section 1. Identification

Identification of the product

Product name: Duloxetine delayed-release capsules USP

Formula: $C_{18}H_{19}NOS \cdot HCl$

Chemical Name: (+)-(*S*)-*N*-methyl-γ-(1-naphthyloxy)-2-thiophenepropylamine hydrochloride.



Duloxetine hydrochloride

Manufacturer / supplier identification

Company: **Cadila Healthcare Ltd. Ahmedabad, India**

Address: Sarkhej – Bavla. N.H. 8A, Moraiya. Tal. Sanand.
Dist. Ahmedabad – 382210. State: Gujarat. India

Contact for information: Tel.: +91 79 6868100 Fax: +91 79 3750319

Emergency Telephone No. Tel.: +91 79 6868100

Recommended Use / Therapeutic Category Selective serotonin and norepinephrine reuptake inhibitor (SSNRI)

Restriction on Use / Contraindications Serotonin Syndrome and MAOIs: Do not use MAOIs intended to treat psychiatric disorders with duloxetine or within 5 days of stopping treatment with duloxetine. Do not use duloxetine within 14 days of stopping an MAOI intended to treat psychiatric disorders.

In addition, do not start duloxetine in a patient who is being treated with linezolid or intravenous methylene blue. Use in patients with uncontrolled narrow-angle glaucoma.

Section 2. Hazard(s) Identification

Dose and Administration

Duloxetine delayed-release capsules should be swallowed whole and should not be chewed or crushed, nor should the capsule be opened and its contents sprinkled on food or mixed with liquids. All of these might affect the enteric coating. Duloxetine delayed-release capsules can be given without regard to meals.

Adverse Effects

Most common adverse reactions are nausea, dry mouth, somnolence, constipation, decreased appetite and hyperhidrosis.

Over Dose Effect

Signs and symptoms of overdose (duloxetine alone or with mixed drugs) included somnolence, coma, serotonin syndrome, seizures, syncope, tachycardia, hypotension, hypertension and vomiting.

Medical Conditions

Before starting duloxetine delayed-release capsules, tell your healthcare provider if you are taking certain drugs such as: Triptans used to treat migraine headache, Medicines used to treat mood, anxiety, psychotic or thought disorders, including tricyclics, lithium, buspirone, SSRIs, SNRIs or MAOIs , Tramadol and fentanyl , Cimetidine , antibiotics ciprofloxacin, enoxacin, Medicine to control heart rate such as propafenone, flecainide, quinidine , Theophylline , blood thinner warfarin (Coumadin®*, Jantoven®*) , Non-steroidal anti-inflammatory drug (NSAID), like ibuprofen, naproxen or aspirin , Over-the-counter supplements such as tryptophan or St. John's Wort , have heart problems or high blood pressure , have diabetes (duloxetine delayed-release capsules treatment worsens the control of blood sugar in some patients with diabetes) , have liver problems , have kidney problems , have glaucoma , have or had seizures or convulsions , have bipolar disorder or mania , have low sodium levels in your blood , have delayed stomach emptying , have or had bleeding problems , are pregnant or plan to become pregnant. It is not known if duloxetine delayed-release capsules will harm your unborn baby. Talk to your healthcare provider about the benefits and risks of treating depression or other conditions with duloxetine delayed-release capsules during pregnancy , are breastfeeding or plan to breastfeed. Some duloxetine may pass into your breast milk. Talk to your healthcare provider about the best way to feed your baby while taking duloxetine delayed-release capsules.

Tell your healthcare provider about all the medicines that you take, including prescription and non-prescription medicines, vitamins, and herbal supplements. Duloxetine delayed-release capsules and some medicines may interact with each other, may not work as well, or may cause serious side effects.

Your healthcare provider or pharmacist can tell you if it is safe to take duloxetine delayed-release capsules with your other medicines. Do not start or stop any medicine while taking duloxetine delayed-release capsules without talking to your healthcare provider first.

If you take duloxetine delayed-release capsules, you should not take any other medicines that contain duloxetine.

Contraindications Serotonin Syndrome and MAOIs: Do not use MAOIs intended to treat psychiatric disorders with duloxetine or within 5 days of stopping treatment with duloxetine. Do not use duloxetine within 14 days of stopping an MAOI intended to treat psychiatric disorders. In addition, do not start duloxetine in a patient who is being treated with linezolid or intravenous methylene blue.
Use in patients with uncontrolled narrow-angle glaucoma.

Pregnancy Comments Pregnancy and Nursing Mothers: Use only if the potential benefit justifies the potential risk to the fetus or child

Pregnancy Category C

Section 3. Composition / information on ingredients

Component	Exposure Limit	CAS No.
Principle Component :		
Duloxetine hydrochloride	Not Found	136434-34-9
Inactive Ingredients :		
FD&C blue # 1	Not Found	NA
Hypromellose,	Not Found	9004-65-3
Hypromellose phthalate	Not Found	9050-31-1
Sodium lauryl sulfate	Not Found	151-21-3
Gelatin	Not Found	9000-70-8
Sucrose	Not Found	57-50-1
Sugar spheres	Not Found	NA
Talc	Not Found	14807-96-6
Titanium dioxide	Not Found	13463-67-7
Triethyl citrate	Not Found	77-93-0
D&C yellow # 10 (For 20 mg)	Not Found	NA
FD&C yellow # 6 (For 20 mg)	Not Found	NA
D&C yellow # 10 (For 30 mg)	Not Found	NA
FD&C red # 40 (For 30 mg)	Not Found	NA

FD&C yellow # 6 (For 30 mg)	Not Found	NA
FD&C red # 40 (For 60 mg)	Not Found	NA

Section 4. First -aid measures

General

Inhalation

Remove to fresh air. If not breathing give artificial respiration. If breathing is difficult, give oxygen. Seek medical attention.

contact with skin

Immediately wash skin with soap and copious amounts of water for at least 15 minutes. If irritation persists, seek medical attention.

Ingestion

If swallowed, wash out mouth with water, provided person is concious. Seek medical advice

Remove and wash/dispose of contaminated clothing promptly.

Overdose Treatment

There is no specific antidote to duloxetine, but if serotonin syndrome ensues, specific treatment (such as with cyproheptadine and/or temperature control) may be considered. In case of acute overdose, treatment should consist of those general measures employed in the management of overdose with any drug.

An adequate airway, oxygenation, and ventilation should be assured, and cardiac rhythm and vital signs should be monitored. Induction of emesis is not recommended. Gastric lavage with a large-bore orogastric tube with appropriate airway protection, if needed, may be indicated if performed soon after ingestion or in symptomatic patients.

Activated charcoal may be useful in limiting absorption of duloxetine from the gastrointestinal tract. Administration of activated charcoal has been shown to decrease AUC and C_{max} by an average of one-third, although some subjects had a limited effect of activated charcoal. Due to the large volume of distribution of this drug, forced diuresis, dialysis, hemoperfusion, and exchange transfusion are unlikely to be beneficial.

In managing overdose, the possibility of multiple drug involvement should be considered. A specific caution involves patients who are taking or have recently taken duloxetine and might ingest excessive quantities of a TCA. In such a case, decreased clearance of the parent tricyclic and/or its active metabolite may increase the possibility of clinically significant sequelae and extend the time needed for close medical observation. The physician should consider contacting a poison control center for additional information on the treatment of any 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. 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

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 duloxetine delayed-release capsules at 20° to 25°C (68° to 77°F)
Dispense in a tight container.

Incompatibility: Reactive with acids, alkalis.

Section 8. Exposure controls / 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

Duloxetine Delayed-release Capsules, USP equivalent to 20 mg of duloxetine are white to off-white free flowing pellets filled in size '4' hard gelatin capsules with green colored cap printed with "385" in golden ink and white body printed with "20 mg" in golden ink

Duloxetine Delayed-release Capsules, USP equivalent to 30 mg of duloxetine are white to off-white free flowing pellets filled in size '3' hard gelatin capsules with blue-colored cap printed with "386" in golden ink and green-colored body printed with "30 mg" in golden ink

Duloxetine Delayed-release Capsules, USP equivalent to 60 mg of duloxetine are white to off-white free flowing pellets filled in size '1' hard gelatin capsules with blue-colored cap printed with "387" in golden ink and white-colored body printed with "60 mg" in golden ink

Solubility	Freely soluble in methanol, practically insoluble in hexane, sparingly soluble in water.	**Odour**	No Data Available
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

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	Reactive with acids, alkalis.		

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 specifie formulation.

Target organ

Eye contact, Skin contact and inhalation is not great risk as this product is Capsule.

Other

Carcinogenesis

Duloxetine was administered in the diet to mice and rats for 2 years.

In female mice receiving duloxetine at 140 mg/kg/day (11 times the maximum recommended human dose [MRHD, 60 mg/day] and 6 times the human dose of 120 mg/day on a mg/m^2 basis), there was an increased incidence of hepatocellular adenomas and carcinomas. The no-effect dose was 50 mg/kg/day (4 times the MRHD and 2 times the human dose of 120 mg/day on a mg/m^2 basis). Tumor incidence was not increased in male mice receiving duloxetine at doses up to 100 mg/kg/day (8 times the MRHD and 4 times the human dose of 120 mg/day on a mg/m^2 basis).

In rats, dietary doses of duloxetine up to 27 mg/kg/day in females (4 times the MRHD and 2 times the human dose of 120 mg/day on a mg/m^2 basis) and up to 36 mg/kg/day in males (6 times the MRHD and 3 times the human dose of 120 mg/day on a mg/m^2 basis) did not increase the incidence of tumors.

Mutagenesis

Duloxetine was not mutagenic in the *in vitro* bacterial reverse mutation assay (Ames test) and was not clastogenic in an *in vivo* chromosomal aberration test in mouse bone marrow cells. Additionally, duloxetine was not genotoxic in an *in vitro* mammalian forward gene mutation assay in mouse lymphoma cells or in an *in vitro* unscheduled DNA synthesis (UDS) assay in primary rat hepatocytes, and did not induce sister chromatid exchange in Chinese hamster bone marrow *in vivo*.

Impairment of Fertility

Duloxetine administered orally to either male or female rats prior to and throughout mating at doses up to 45 mg/kg/day (7 times the maximum recommended human dose of 60 mg/day and 4 times the human dose of 120 mg/day on a mg/m^2 basis) did not alter mating or fertility.

Section 12. Ecological information

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

Section 13. Disposal Consideration

Dispose the waste in accordance with all applicable Federal, State and local laws.

Section 14. Transport Information

The product is not hazardous when shipping via air (IATA), ground (DOT), or sea(IMDG).

Section 15. Regulatory Information

Generic Medicine. Approved by USFDA & the ANDA Number is 090739

Section 16. Other information

None

Date of issue: 28/05/2015 **Supersedes edition of:** 01

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.