For the use of a Psychiatrist only

1. GENERIC NAME & BRAND NAME
Desvenlafaxine Extended Release Tablet 25mg
MDD® XR 25

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:
Each film coated extended release tablet contains:
Desvenlafaxine Succinate USP
Equivalent to Desvenlafaxine……25 mg
Colours: Ferric Oxide USP NF Yellow & Titanium Dioxide I.P.

3. DOSAGE FORM AND STRENGTH
Kindly Refer to section 1 & 2

4.CLINICAL PARTICULARS
4.1 THERAPEUTIC INDICATIONS
For the treatment of major depressive disorder (MDD)

4.2 POSOLOGY AND METHOD OF ADMINISTRATION
Recommended dose: 50 mg once daily with or without food. Tablets must be swallowed whole with fluid and not divided, crushed, chewed, or dissolved.
When discontinuing therapy, gradual dose reduction is recommended to minimize discontinuation symptoms. If intolerable symptoms occur after a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the physician may decrease the dose, but at a more gradual rate.

4.3 CONTRAINDICATIONS
Desvenlafaxine is contraindicated in patients with hypersensitivity to desvenlafaxine succinate, venlafaxine hydrochloride or any excipients in the product. The use of desvenlafaxine with an MAOI is not recommended.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

- **Clinical Worsening/ 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 behaviour (suicidality) or unusual changes in behaviour, 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. Pooled analyses of short-term placebo-controlled studies of antidepressant drugs (SSRIs and others) showed that these drugs increase the risk of suicidal thinking and behaviour (suicidality) in children, adolescents, and young adults (ages 18-24) with major depressive disorder (MDD) and other psychiatric disorders. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction with antidepressants compared to placebo in adults aged 65 and older.

- All patients being treated with antidepressants for any indication should be monitored appropriately and observed closely for clinical worsening, suicidality, and unusual changes in behaviour, especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases.
- **Serotonin Syndrome or Neuroleptic Malignant Syndrome (NMS)-like Reactions**: Serotonin syndrome or NMS-like reactions have been reported with SSRIs and SNRIs. NMS may occur particularly with concomitant use of serotonergic drugs (including triptans) with drugs that impair the metabolism of serotonin such as MAOIs, or with antipsychotics or other dopamine antagonists. Serotonin syndrome symptoms may include mental status changes (e.g., agitation, hallucinations, coma), autonomic instability (e.g., tachycardia, labile blood pressure, hyperthermia), neuromuscular aberrations (e.g., hyperreflexia, incoordination) and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea). Therefore, desvenlafaxine should be discontinued & supportive treatment should be initiated.
- **Elevated Blood Pressure**: Monitoring of blood pressure is recommended regularly during treatment. Patients receiving Desvenlafaxine should have regular monitoring of blood pressure since increases in blood pressure were observed in clinical studies. Pre-existing hypertension should be controlled before initiating treatment with Desvenlafaxine. Caution should be exercised in treating patients with pre-existing hypertension or other underlying conditions that might be compromised by increases in blood pressure.
- **Seizure:** Desvenlafaxine has not been systematically evaluated in patients with a seizure disorder. Desvenlafaxine should be prescribed with caution in patients with a seizure disorder.
- **Abnormal Bleeding**: Patients should be cautioned about the risk of bleeding associated with the concomitant use of desvenlafaxine and NSAIDs, aspirin, or other drugs that affect coagulation.
- **Narrow-angle Glaucoma**: Patients with raised intraocular pressure or those at risk of angle-closure glaucoma should be monitored.
- **Activation of Mania/Hypomania**: Use cautiously in patients with bipolar disorder. Adequate screening for bipolar disorder is required before initiating treatment with the drug.
- **Cardiovascular/Cerebrovascular Disease:** Use cautiously in patients with cardiovascular or cerebrovascular disease. Based on the current literature, risk of QT/QTc prolongation with the majority of newer non-SSRI antidepressants at therapeutic doses is low. The highest risk for QT prolongation appears to exist in overdose situations with venlafaxine. Largely because of a lack of available data, existing studies fail to demonstrate QT prolongation with desvenlafaxine
- **Interstitial lung disease and eosinophilic pneumonia:** Rarely, Interstitial lung disease and eosinophilic pneumonia may be associated with venlafaxine (the parent drug of desvenlafaxine) . These patients may present with present with progressive dyspnea, cough, or chest discomfort. Such patients should undergo a prompt medical evaluation, and discontinuation of desvenlafaxine should be considered
- **Cholesterol and Triglyceride Elevation:** Use cautiously in patients with lipid metabolism disorders. Monitoring of serum cholesterol and triglyceride is recommended.
- **Discontinuation Symptoms:** Abrupt discontinuation or dose reduction has been associated with the appearance of new symptoms such as dizziness, nausea, headache, irritability, insomnia, diarrhea, anxiety, fatigue, abnormal dreams, and hyperhidrosis.

In general, discontinuation events occurred more frequently with longer duration of therapy. Patients should be monitored for these symptoms when discontinuing treatment with desvenlafaxine. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered.

- **Renal Impairment:** Dosage adjustment is necessary in severe and ESRD. The recommended dose in patients with severe renal impairment or ESRD is 50 mg every other day. In moderate renal impairment, the dose should not exceed 50 mg/day.
- **Hyponatremia:** Can occur in association with SIADH. Signs and symptoms of hyponatremia include headache, difficulty concentrating, memory impairment, confusion, weakness, and unsteadiness, which can lead to falls. Signs and symptoms associated with more severe and/or acute cases have included hallucination, syncope, seizure, coma, respiratory arrest, and death.
- **Pregnant Women** -Pregnancy Category C: The safety of desvenlafaxine in human pregnancy has not been established.
- **Labour and Delivery**-The effect of desvenlafaxine on labour and delivery in humans is unknown.
- **Nursing Women**- Desvenlafaxine (O-desmethylvenlafaxine, a metabolite of desvenlafaxine) is excreted in human milk.
- **Pediatric**-Safety and effectiveness in patients less than 18 years of age have not been established.
- **Geriatrics (≥ 65 years of age)-**For elderly patients, possible reduced renal clearance of desvenlafaxine should be considered when determining the dose.
- **Interference with Cognitive and Motor Performance:** Caution patients regarding the risks of operating hazardous machinery, including automobiles, until they are certain that desvenlafaxine therapy does not adversely affect their ability to engage in such activities.

4.5 DRUG INTERACTIONS

No	Drug	Drug interaction	Remark
1.	Monoamine Oxidase Inhibitors	Desvenlafaxine succinate must not be used in combination with a monoamine oxidase inhibitor (MAOI), or within at least 14 days of discontinuing treatment with an MAOI. Based on the half-life of desvenlafaxine succinate, at least 7 days should be allowed after stopping desvenlafaxine succinate before starting an MAOI.	Desvenlafaxine succinate is contraindicated in patients taking MAOIs
2.	Central Nervous System (CNS) Active Agents	The risk of using desvenlafaxine succinate in combination with other CNS-active drugs has not been systematically evaluated.	Caution is advised when desvenlafaxine succinate is taken in combination with other CNS-active drugs.

3.	Drugs Affecting Platelet Function (e.g., NSAIDs, ASA, and other anticoagulants)	Altered anticoagulant effects, including increased bleeding, have been reported when SSRIs or SNRIs are co-administered with warfarin	Patients receiving warfarin therapy should be carefully monitored when desvenlafaxine is initiated or discontinued
4.	Electroconvulsive Therapy	There are no clinical data establishing the risks and/or benefits of electroconvulsive therapy	
5	Drugs metabolized by CYP2D6 (desipramine)	Clinical studies have shown that desvenlafaxine does not have a clinically relevant effect on CYP2D6 metabolism at the dose of 100 mg daily. When 400 mg (8 times the recommended 50 mg dose) was administered, the Cmax and AUC of desipramine increased approximately 50% and 90%, respectively.	Concomitant use of desvenlafaxine(at 8 times recommended dose) with a drug metabolized by CYP2D6 can result in higher concentrations of that drug.
6.	Drugs metabolized by CYP3A4 (midazolam)	The AUC and Cmax of midazolam decreased by approximately 31% and 16%, respectively.	Concomitant use of desvenlafaxine with a drug metabolized by CYP3A4 can result in lower exposures to that drug.
7.	Alcohol	Desvenlafaxine does not increase the impairment of mental and motor skills caused by ethanol.	As with all CNS-active drugs, patients should be advised to avoid alcohol consumption while taking desvenlafaxine

Drug-Laboratory Test Interactions

False-positive urine immunoassay screening tests for phencyclidine (PCP) and amphetamine have been reported in patients taking desvenlafaxine. This may be attributed to lack of specificity of the screening tests.

Statistically significant increases from baseline to end point were observed for the following laboratory values: alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT), bilirubin alkaline phosphatase, fasting total cholesterol, and fasting triglycerides. In general, these changes were not clinically significant.

4.6 USE IN SPECIAL POPULATIONS (SUCH AS PREGNANT WOMEN, LACTATING WOMEN, PAEDIATRIC PATIENTS, GERIATRIC PATIENTS ETC.)

Pregnancy
There are no adequate and well-controlled studies in pregnant women. Therefore, it should be used during pregnancy only if the potential benefits justify the potential risks.
Neonates exposed to SNRIs (Serotonin and Norepinephrine Reuptake Inhibitors), or SSRIs (Selective Serotonin Reuptake Inhibitors), late in the third trimester have developed complications requiring prolonged hospitalization, respiratory support, and tube feeding. Such complications can arise immediately upon delivery. Reported clinical findings have included respiratory distress, cyanosis, apnea, seizures, temperature instability, feeding difficulty, vomiting, hypoglycemia, hypotonia, hypertonia, hyperreflexia, tremor, jitteriness, irritability, and constant crying. These features are consistent with either a direct toxic effect of SSRIs and SNRIs or, possibly, a drug discontinuation syndrome. It should be noted that, in some cases, the clinical picture is consistent with serotonin syndrome. When treating a pregnant woman during the third trimester, the physician should carefully consider the potential risks and benefits of treatment.

Lactating woman
Desvenlafaxine (O-desmethylvenlafaxine) is excreted in human milk. Because of the potential for serious adverse reactions in nursing infants, a decision should be made whether or not to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. Only administer to breastfeeding women if the expected benefits outweigh any possible risk.

Pediatric
Safety and effectiveness in the pediatric population have not been established.

Geriatric
Of the 3,292 patients in clinical studies, 5% were 65 years of age or older. No overall differences in safety or efficacy were observed between these patients and younger patients; however, in the short-term, placebo-controlled studies, there was a higher incidence of systolic orthostatic hypotension in patients ≥ 65 years of age compared to patients < 65 years of age treated with desvenlafaxine.
For elderly patients, possible reduced renal clearance of desvenlafaxine should be considered when determining dose and Clinical Pharmacology. If poorly tolerated, every other day dosing can be considered. SSRIs and SNRIs, have been associated with cases of clinically significant hyponatremia in elderly patients, who may be at greater risk for this adverse event. Greater sensitivity of some older individuals cannot be ruled out.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES
Caution patients about operating hazardous machinery, including automobiles, until they are reasonably certain that therapy does not adversely affect their ability to engage in such activities.

4.8 UNDESIRABLE EFFECTS
- **Gastrointestinal disorders:** Nausea, dry mouth, constipation, Vomiting, diarrhea.
- **Cardiac disorders:** Palpitations, tachycardia, Several small but statistically significant changes in electrocardiogram (ECG) intervals were observed, most of which were attributable to increases in heart rate (shortening of PR and QRS intervals).
- **Ear and labyrinth disorders:** Tinnitus.
- **Eye disorders:** Mydriasis, vision blurred.

- **Biochemistry changes**: elevated blood cholesterol, raised blood prolactin levels, increased, increased blood triglycerides, abnormal liver function test.
- **Metabolism and nutrition disorders:** Decreased appetite, weight changes Rare: hyponatremia.
- **Musculoskeletal, connective tissue, and bone disorders**: Musculoskeletal stiffness.
- **General disorders**: Fatigue; Asthenia, chills, feeling jittery, irritability; Drug withdrawal syndrome.
- Im**mune system disorders:** Hypersensitivity.
- **Nervous system disorders**: headache, dizziness; Common: somnolence, tremor, disturbance in attention, paraesthesia, dysgeusia; Uncommon: syncope; Rare: convulsion, dystonia.
- **Psychiatric disorders**: Very common: insomnia; Common: orgasm abnormal, anorgasmia, anxiety, nervousness, libido decreased, abnormal dreams; Uncommon: depersonalization, hypomania, bruxism.
- **Vascular disorders**: Common: hot flush; Uncommon: orthostatic hypotension, peripheral coldness, increases in blood pressure.
- **Renal and urinary disorders**: Common: urinary hesitation; Uncommon: urinary retention; Rare: proteinuria.
- **Reproductive system and breast disorders**: Common: erectile dysfunction, ejaculation delayed, ejaculation disorder, ejaculation failure; Uncommon: sexual dysfunction, Persistent sexual dysfunction after drug withdrawal.
- **Respiratory, thoracic, and mediastinal disorders**: Yawning; Epistaxis.
- **Skin and subcutaneous tissue disorders**: Very common: hyperhidrosis; Common: rash; Uncommon: alopecia; Rare: angioedema.

4.9 OVERDOSAGE

There is limited clinical trial experience with desvenlafaxine succinate overdosage in humans. The most commonly reported events in overdosage with venlafaxine (the parent compound) include tachycardia, changes in level of consciousness (ranging from somnolence to coma), mydriasis, seizures, and vomiting. Electrocardiogram changes (e.g.prolongation of QT interval, bundle branch block, QRS prolongation), sinus and ventricular tachycardia, bradycardia, hypotension, rhabdomyolysis, vertigo, liver necrosis, serotonin syndrome, and death have been reported.

There is no specific antidote for desvenlafaxine. Symptomatic and supportive therapy must be instituted.

5. PHARMACOLOGIC PROPERTIES

5.1 MECHANISM OF ACTION

Non-clinical studies have shown that desvenlafaxine succinate is a potent and selective serotonin and norepinephrine reuptake inhibitor (SNRI). The clinical efficacy of desvenlafaxine succinate is thought to be related to the potentiation of these neurotransmitters in the central nervous system.

5.2 PHARMACODYNAMIC PROPERTIES

Desvenlafaxine succinate, a serotonin-norepinephrine reuptake inhibitor (SNRI), is a newer antidepressant, which inhibits serotonin-norepinephrine reuptake neurotransmission.

Desvenlafaxine is the active metabolite of venlafaxine.

Desvenlafaxine inhibits the reuptake of both norepinephrine and serotonin at the starting dose. Dual reuptake inhibitors have been shown to have small but statistically significantly greater rates of response and remission compared to selective serotonin reuptake inhibitors.
In clinical trials, after eight weeks of treatment, the mean HAM-D17 scores for desvenlafaxine 100 mg per day and 400 mg per day were significantly lower than for placebo Desvenlafaxine significantly improved psychological well-being.
In *in vitro* studies, Desvenlafaxine lacked significant affinity for numerous receptors, including muscarinic, cholinergic, alpha(α) 1-adrenergic receptors in vitro. Desvenlafaxine also lacked H1-histaminergic or significant affinity for various ion channels, including calcium, chloride, potassium and sodium ion channels and also lacked monoamine oxidase (MAO) inhibitory activity. Desvenlafaxine lacked significant activity in the in vitro cardiac potassium channel (hERG) assay.

5.3 PHARMACOKINETIC PROPERTIES

Parameters	**Desvenlafaxine**
Absorption	The absolute oral bioavailability of desvenlafaxine is about 80%. Mean time to peak plasma concentrations (tmax) is about 7.5 hours after oral administration
Metabolism	Desvenlafaxine is primarily metabolized by conjugation (mediated by UGT isoforms) and, to a minor extent, through oxidative metabolism. CYP3A4 is the cytochrome P450 isozyme mediating the oxidative metabolism (N-demethylation) of desvenlafaxine
Excretion	Approximately 45% of desvenlafaxine is excreted unchanged in urine at 72 hours after oral administration.
Half life	The mean terminal half-life, t1/2, is approximately 11 hours

6. NONCLINICAL PROPERTIES

6.1 ANIMAL TOXICOLOGY OR PHARMACOLOGY

When desvenlafaxine succinate was administered orally to pregnant rats and rabbits during the period of organogenesis, there was no evidence of teratogenicity in rats at any doses tested, up to 10 times a human dose of 100 mg/day (on a mg/m2 basis) in rats, and up to 15 times a human dose of 100 mg/day (on a mg/m2 basis) in rabbits. However, fetal weights were decreased in rats, with a no-effect dose 10 times a human dose of 100 mg/day (on a mg/m2 basis). When desvenlafaxine succinate was administered orally to pregnant rats throughout gestation and lactation, there was a decrease in pup weights and an increase in pup deaths during the first four days of lactation. The cause of these deaths is not known. The no-effect dose for rat pup mortality was 10 times a human dose of 100 mg/day (on a mg/m2 basis). Post-weaning growth and reproductive performance of the progeny were not affected by maternal treatment with desvenlafaxine at a dose 29 times a human dose of 100 mg/day (on a mg/m2 basis)

Carcinogenesis

Desvenlafaxine succinate administered by oral gavage to mice and rats for 2 years did not increase the incidence of tumors in either study. Mice received desvenlafaxine succinate at dosages up to 500/300 mg/kg/day (dosage lowered after 45 weeks of dosing). The 300 mg/kg/day dose is 15 times a human dose of 100 mg/day on a mg/m2 basis. Rats received desvenlafaxine succinate at dosages up to 300 mg/kg/day (males) or 500 mg/kg/day (females).

The highest dose is 29 (males) or 48 (females) times a human dose of 100 mg/day on a mg/m2 basis.

Mutagenesis
Desvenlafaxine was not mutagenic in the in vitro bacterial mutation assay (Ames test) and was not clastogenic in an in vitro chromosome aberration assay in cultured CHO cells, an in vivo mouse micronucleus assay, or an in vivo chromosome aberration assay in rats. Additionally, desvenlafaxine was not genotoxic in the in vitro CHO mammalian cell forward mutation assay and was negative in the in vitro BALB/c-3T3 mouse embryo cell transformation assay.
Impairment of fertility Reduced fertility was observed in a study in which both male and female rats received desvenlafaxine succinate. This effect was noted at oral doses approximately 10 times a human dose of 100 mg/day on a mg/m2 basis. There was no effect on fertility at oral doses approximately 3 times a human dose of 100 mg/day on a mg/m2 basis

7. DESCRIPTION
MDD XR 25 is supplied for oral administration, as a extended - release tablet of Desvenlafaxine. Each film coated extended - release tablet of MDD XR 25 contains Desvenlafaxine Succinate equivalent to Desvenlafaxine 25 mg.

8. PHARMACEUTICAL PARTICULARS
8.1 INCOMPATIBILITIES
Not Applicable

8.2 SHELF-LIFE
Refer Pack

8.3 PACKAGING INFORMATION
Refer Pack

8.4 STORAGE AND HANDING INSTRUCTIONS
Refer Pack

9. PATIENT COUNSELLING INFORMATION
50 mg once daily with or without food. When discontinuing therapy, gradual dose reduction is recommended to minimize discontinuation symptoms. If intolerable symptoms occur after a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the physician may decrease the dose, but at a more gradual rate.
Desvenlafaxine is contraindicated in patients with hypersensitivity to desvenlafaxine succinate, venlafaxine hydrochloride or any excipients in the product. The use of desvenlafaxine with an MAOI is not recommended. (Kindly refer to Details in section 4.4)

10. DETAILS OF MANUFACTURER
Refer pack for manufacturer details.

Marketed By:
Abbott Healthcare Pvt. Ltd.
Angel Space, Bldg. D-4, Gala No. l to 3 & 11 to 13
Ground Floor, 101 lo 106 & 111 to 116 First Floor,
201 to 206 & 211 to 216 2nd Floor, Pimplas,

Version: 5.0, dated 18th June 2025
Replaces Version: 4.0, Dated: 1st Oct 2024

Dist. Thane, Bhiwandi - 421 302,
Maharashtra, India.

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11. DETAILS OF PERMISSION OR LICENCE NUMBER WITH DATE
Refer Pack for Permission/License details.

12. DATE OF REVISION
Version: 5.0, Dated: 18th June 2025

For Product Complaints/Adverse events or Queries please write to
webmasterindia@abbott.com