Lafaxine® ER
(D e s v e n l a f a x i n e)
Tablets

50mg
100mg

لیفکزین ای آر ۵۰ ملی گرام
(ڈیسوین لیفکزین) ۱۰۰ ملی گرام
ٹیبلٹس

QUALITATIVE AND QUANTITATIVE COMPOSITION

Lafaxine® ER Tablets 50mg
Each extended-release tablet contains:
Desvenlafaxine as Succinate.....50mg
Genix Specification
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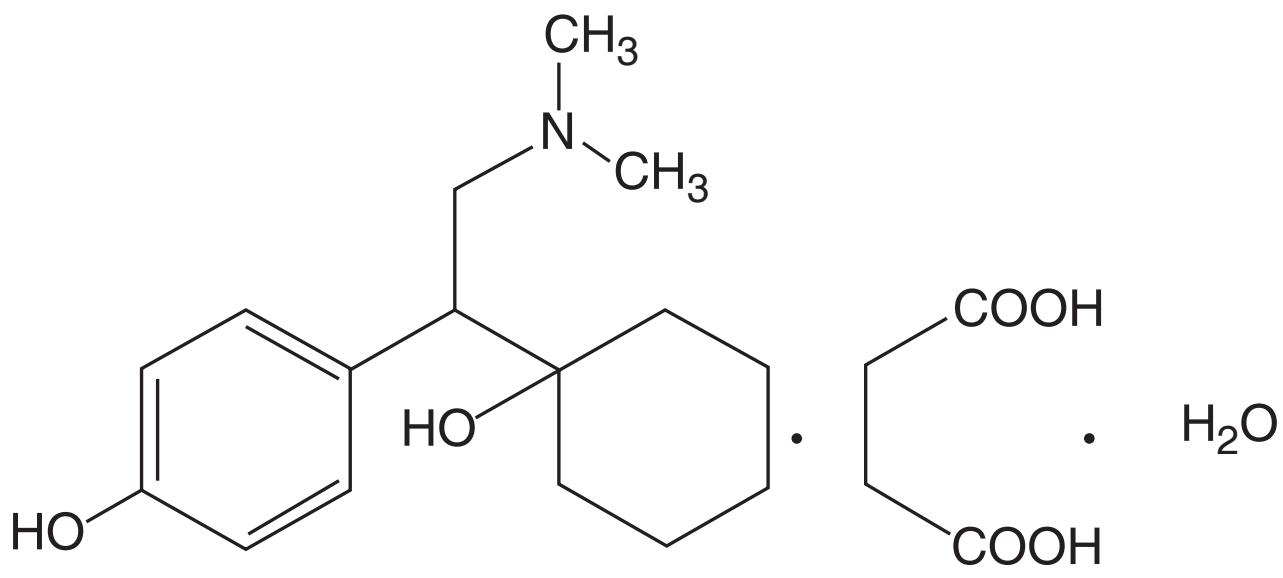
DESCRIPTION:

Desvenlafaxine is an extended-release tablet for oral administration that contains desvenlafaxine succinate, a Desvenlafaxine is designated RS-4-[2-dimethylamino-1 -(1 -hydroxycyclohexyl) ethyl] phenol and has the empirical formula of C16H25NO2C4H6O4.H2O (Desvenlafaxine succinate monohydrate). Desvenlafaxine succinate monohydrate has a molecular weight of 399.48. The structural formula is shown below.



CLINICAL PHARMACOLOGY:

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.

Pharmacodynamics:
Desvenlafaxine lacked significant affinity for numerous receptors, including muscarinic-cholinergic, Hi-histaminergic, or ai-adrenergic receptors in vitro. Desvenlafaxine also lacked monoamine oxidase (MAO) inhibitory activity.

Pharmacokinetics:
The single-dose pharmacokinetics of desvenlafaxine are linear and dose-proportional in a dose range of 100 to 600 mg/day. The mean terminal half-life, t½, is approximately 11 hours. With once-daily dosing,

steady-state plasma concentrations are achieved within approximately 4-5 days. At steady-state, multiple-dose accumulation of desvenlafaxine is linear and predictable from the single-dose pharmacokinetic profile.

Absorption and Distribution:
The absolute oral bioavailability of Desvenlafaxine after oral administration is about 80%. Mean time to peak plasma concentrations (Tmax) is about 7.5 hours after oral administration. A food-effect study involving administration of Desvenlafaxine (desvenlafaxine extended-release tablets) to healthy subjects under fasting and fed conditions (high-fat meal) indicated that the Cmax was increased about 16% in the fed state, while the AUCs were similar. This difference is not clinically significant; therefore, Desvenlafaxine can be taken without regard to meals. The plasma protein binding of desvenlafaxine is low (30%) and is independent of drug concentration.

Metabolism and Elimination:
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. The CYP2D6 metabolic pathway is not involved, and after administration of 100 mg, the pharmacokinetics of desvenlafaxine was similar in subjects with CYP2D6 poor and extensive metabolizer phenotype. Approximately 45% of desvenlafaxine is excreted unchanged in urine at 72 hours after oral administration. Approximately 19% of the administered dose is excreted as the glucuronide metabolite and < 5% as the oxidative metabolite (N,O-didesmethylvenlafaxine) in urine.

INDICATIONS:
Desvenlafaxine a selective serotonin and norepinephrine re-uptake inhibitor (SNRI) is indicated for the treatment of major depressive disorder (MDD). A major depressive episode (DSM-IV) implies a prominent and relatively persistent (nearly every day for at least 2 weeks) depressed or dysphoric mood that usually interferes with daily functioning, and includes at least 5 of the following 9 symptoms: depressed mood, loss of interest in usual activities, significant change in weight and/or appetite, insomnia or hypersomnia, psychomotor agitation or retardation, increased fatigue, feelings of guilt or worthlessness, slowed thinking or impaired concentration, or a suicide attempt or suicidal ideation.

DOSAGE AND ADMINISTRATION:
Initial Treatment of Major Depressive Disorder:
The recommended dose for Lafaxine ER (desvenlafaxine extended-release tablets) is 50 mg once daily, with or without food. When discontinuing therapy, gradual dose reduction is recommended whenever possible to minimize discontinuation symptoms. Lafaxine ER (desvenlafaxine extended-release tablets) should be taken at approximately the same time each day. Tablets must be swallowed whole with fluid and not divided, crushed, chewed, or dissolved.

Special Populations:
Pregnant women during the third trimester:
Neonates exposed to SNRIs or SSRIs late in the third trimester have developed complications requiring prolonged hospitalization, respiratory support and tube feeding. When treating pregnant women with Lafaxine ER (desvenlafaxine extended-release tablets) during the third trimester, the physician should carefully consider the potential risks and benefits of

treatment. The physician may consider tapering Lafaxine ER (desvenlafaxine extended-release tablets) in the third trimester.

Patients with renal impairment:

No dosage adjustment is necessary in patients with mild renal impairment (24-hr CrCl = 50-80 mL/min). The recommended dose in patients with moderate renal impairment is 50 mg per day. The recommended dose in patients with severe renal impairment or end-stage renal disease (ESRD) is 50 mg every other day.

Patients with hepatic impairment:

The recommended dose in patients with hepatic impairment is 50 mg/day. Dose escalation above 100 mg/day is not recommended.

Elderly patients: No dosage adjustment is required solely on the basis of age; however, the possibility of reduced renal clearance of Lafaxine ER (desvenlafaxine extended-release tablets) should be considered when determining the dose.

SIDE EFFECTS

The possible side effects of Desvenlafaxine are.

- Hypersensitivity
- Effects on blood pressure
- Abnormal bleeding
- Mydriasis
- Hypomania and mania.
- Serum cholesterol and triglyceride elevation
- Seizure

The most common adverse reactions leading to discontinuation in at least 2% of the desvenlafaxine extended-release tablets treated patients in the short-term studies, up to 8 weeks, were: nausea (4%); dizziness, headache and vomiting (2% each); in the long-term study, up to 9 months, the most common was vomiting (2%).

DRUG INTERACTIONS:

Central Nervous System (CNS)-Active Agents:

The risk of using desvenlafaxine extended-release tablets in combination with other CNS-active drugs has not been systematically evaluated. Consequently, caution is advised when desvenlafaxine extended-release tablets is taken in combination with other CNS-active drugs Monoamine Oxidase Inhibitors (MAOI)'s Adverse reactions, some of which were serious, have been reported in patients who have recently been discontinued from a monoamine oxidase inhibitor (MAOI) and started on antidepressants with pharmacological properties similar to Desvenlafaxine (SNRIs or SSRIs), or who have recently had SNRI or SSRI therapy discontinued prior to initiation of an MAOI.

OVERDOSE:

Human Experience with Overdosage:

There is limited clinical experience with desvenlafaxine succinate overdosage in humans. In pre-marketing clinical studies, no cases of fatal acute overdose of desvenlafaxine were reported.

CONTRAINDICATIONS:

Hypersensitivity:

Hypersensitivity to desvenlafaxine succinate, venlafaxine hydrochloride or to any excipients in the desvenlafaxine extended-release tablets formulation.

Monoamine Oxidase Inhibitors:
Desvenlafaxine extended-release tablets must not be used concomitantly in patients taking monoamine oxidase inhibitors (MAOIs) or in patients who have taken MAOIs within the preceding 14 days.

PRECAUTIONS:

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.

INSTRUCTIONS:

Dosage as directed by the physician.
Store below 30°C.
Protect from heat, light and moisture.
Keep all medicines out of the reach of children.

PRESENTATION:

Lafaxine® ER 50mg (Desvenlafaxine) is available in Alu/Alu blister pack of 1x14's tablets.
Lafaxine® ER 100mg (Desvenlafaxine) is available in Alu/Alu blister pack of 1x14's tablets.

ہدایات:

خوراک ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
۳۰ ڈگری سینٹی گریڈ سے کم پر رکھیں۔
روشنی، گرمی اور نمی سے محفوظ رکھیں۔
تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔

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