Faxine® & Faxine®-SR

(Venlafaxine 50mg Tablet) (Venlafaxine 75mg Capsule)

فیکسِن اور فیکسِن-ایس آر

(وینلافیکسین ۵۰ ملی گرام ٹیبلٹ) (وینلافیکسین ۷۵ ملی گرام کیپسول)

COMPOSITION

Faxine-SR 75mg Capsules

Each capsule contains:

Sustained release pellets of Venlafaxine HCl (BP) equivalent to Venlafaxine 75mg

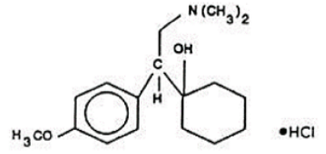
Faxine 50mg Tablets

Each film coated tablet contains:

Venlafaxine HCl (BP) equivalent to Venlafaxine 50mg

DESCRIPTION

Venlafaxine is a structurally novel antidepressant for oral administration. It is designated (R/S)-1-[2-(dimethylamino)-1-(4-methoxyphenyl)ethyl] cyclohexanol hydrochloride or (±)-1-[α-[(dimethyl-amino)methyl]-p-methoxybenzyl]cyclohexanol hydrochloride and has the empirical formula of $C_{17}H_{27}NO_2$ HCl Its molecular weight is 313.87. The structural formula is shown below.



CLINICAL PHARMACOLOGY

Mechanism Of Action

The exact mechanism of the antidepressant action of venlafaxine in humans is unknown, but is thought to be related to the potentiation of serotonin and norepinephrine in the central nervous system, through inhibition of their reuptake. Preclinical studies have shown that venlafaxine and its active metabolite, O-desmethyl venlafaxine (ODV), are potent inhibitors of neuronal serotonin and norepinephrine reuptake and weak inhibitors of dopamine reuptake.

Pharmacokinetics

Venlafaxine is well absorbed and extensively metabolized in the liver. O-desmethyl venlafaxine (ODV) is the only major active metabolite. Renal elimination of venlafaxine and its metabolites is the primary route of excretion. The relative bioavailability of venlafaxine from a tablet was 100% when compared to an oral solution.

The degree of binding of venlafaxine to human plasma is 27% ± 2% at concentrations ranging from 2.5 to 2215 ng/mL.

Approximately 87% of a venlafaxine dose is recovered in the urine within 48 hours as either unchanged venlafaxine (5%), unconjugated ODV (29%), conjugated ODV (26%), or other minor inactive metabolites (27%).

INDICATIONS

Venlafaxine is indicated for the treatment of major depressive disorder.

DOSAGE AND ADMINISTRATION

Usual Adult Dose for Depression

Immediate release

Initial dose: 37.5mg orally twice a day or 25mg orally 3 times a day

Maintenance dose: May increase in daily increments of up to 75mg at intervals of no less than 4 days

Maximum dose (moderately depressed outpatients): 225mg/day

Maximum dose (severely depressed inpatients): 375mg/day

Daily dosage may be divided in 2 or 3 doses/day

Extended Release

Initial dose: 75mg orally once daily

Maintenance dose: May increase in daily increments of up to 75mg at intervals of no less than 4 days

Maximum dose (moderately depressed outpatients): 225mg/day

Maximum dose (severely depressed inpatients): 375mg/day

Usual Adult Dose for Anxiety

For generalized anxiety disorder or social anxiety disorder

Extended release

Initial dose: 75mg orally once daily

Maintenance dose: May increase in daily increments of 75mg at intervals of no less than 4 days

Maximum dose: 225mg/day

Usual Adult Dose for Panic Disorder

Extended-release

Initial dose: 37.5mg once a day

Maintenance dose: May increase dose in daily increments of 75mg at intervals of no less than 7 days

Maximum dose: 225mg/day

SPECIAL POPULATIONS

Treatment Of Pregnant Women During the Third Trimester

Neonates exposed to venlafaxine tablets, other SNRIs, or SSRIs, late in the third trimester have developed complications requiring prolonged hospitalization, respiratory support, and tube feeding. The physician should carefully consider the potential risks and benefits of treatment.

Dosage For Patients With Hepatic Impairment

Given the decrease in clearance and increase in elimination half-life for both venlafaxine and ODV that is observed in patients with hepatic cirrhosis and mild and moderate hepatic impairment compared to normal subjects . Since there was much individual variability in clearance between subjects with cirrhosis, it may be necessary to reduce the dose even more than 50%.

Dosage For Patients With Renal Impairment

Given the decrease in clearance for venlafaxine and the increase in elimination half-life. It is recommended that the total daily dose be reduced by 25% in patients with mild to moderate renal impairment. It is recommended that the total daily dose be reduced by 50% in patients undergoing hemodialysis.

Dosage for Elderly Patients

No dose adjustment is recommended for elderly patients on the basis of age.

Maintenance Treatment

It is generally agreed that acute episodes of major depressive disorder require several months or longer of sustained pharmacological therapy beyond response to the acute episode.

Discontinuing Venlafaxine

Symptoms associated with discontinuation of venlafaxine, other SNRIs, and SSRIs, have been reported.A gradual reduction in the dose rather than abrupt cessation is recommended.

SIDE-EFFECTS

Body as a whole: Headache, Asthenia, Infections, Chills, Chest pain

Cardiovascular: Vasodilation, Hypertension, Tachycardia, Postural Hypotension

Gastrointestinal: Constipation, Anorexia, Diarrhea, Vomiting, Dyspepsia, Nausea

Nervous System: Somnolence, Dry mouth, Dizziness, Insomnia, Nervousness, Anxiety.

DRUG INTERACTIONS

Alcohol

A single dose of ethanol (0.5g/kg) had no effect on the pharmacokinetics of venlafaxine.

Cimetidine

Concomitant administration of cimetidine and venlafaxine in a steady-state study for both drugs resulted in inhibition of first-pass metabolism of venlafaxine .The oral clearance of venlafaxine was reduced by about 43%, and the exposure (AUC) and maximum concentration (Cmax) of the drug were increased by about 60%. The overall pharmacological activity of venlafaxine plus ODV is expected to increase only slightly, and no dosage adjustment should be necessary for most normal adults.

Diazepam

Venlafaxine also did not have any effect on the pharmacokinetics of diazepam or its active metabolite, desmethyl diazepam, or affect the psychomotor and psychometric effects induced by diazepam.

Haloperidol

Venlafaxine administered under steady-state conditions at 150mg/day in 24 healthy subjects decreased total oral-dose clearance (Cl/F) of a single 2mg dose of haloperidol by 42%, which resulted in a 70% increase in haloperidol AUC.

Lithium

The steady-state pharmacokinetics of venlafaxine administered at 150mg/day were not affected when a single 600mg oral dose of lithium was administered. Venlafaxine had no effect on the pharmacokinetics of lithium.

Drugs That Interfere with Hemostasis (e.g., NSAIDs, Aspirin, and Warfarin)

Altered anticoagulant effects, including increased bleeding, have been reported when SSRIs and SNRIs are coadministered with warfarin. Patients receiving warfarin therapy should be carefully monitored when venlafaxine tablets is initiated or discontinued.

Drugs That Inhibit Cytochrome P450 Isoenzymes

CYP2D6 Inhibitors

The potential exists for a drug interaction between drugs that inhibit CYP2D6-mediated metabolism and venlafaxine resulting in higher plasma concentrations of venlafaxine and lower plasma concentrations of ODV.

Ketoconazole

A pharmacokinetic study with ketoconazole 100mg b.i.d. with a single dose of venlafaxine 50mg in extensive metabolizers resulted in higher plasma concentrations of both venlafaxine and O-desvenlafaxine (ODV) in most subjects following administration of ketoconazole.

Drugs Metabolized By Cytochrome P450 Isoenzymes

Imipramine

Venlafaxine did not affect the pharmacokinetics of imipramine.

Metoprolol

Concomitant administration of venlafaxine (50mg every 8 hours for 5 days) and metoprolol increase of plasma concentrations of metoprolol by approximately 30 to 40%.

Risperidone

Venlafaxine administered under steady-state conditions at 150mg/day slightly inhibited the CYP2D6- mediated metabolism of risperidone.

WARNINGS

Serotonin Syndrome

The development of a potentially life-threatening serotonin syndrome has been reported with SNRIs and SSRIs, including venlafaxine. The concomitant use of venlafaxine with MAOIs intended to treat psychiatric disorders is contraindicated.

Angle-Closure Glaucoma

The pupillary dilation that occurs following use of many antidepressant drugs including venlafaxine may trigger an angle closure attack in a patient with anatomically narrow angles who does not have a patent iridectomy.

Sustained Hypertension

Venlafaxine treatment is associated with sustained increases in blood pressure in some patients

Mydriasis

Mydriasis has been reported in association with venlafaxine; therefore, patients at risk of acute narrow angle glaucoma (angle-closure glaucoma) should be monitored.

PRECAUTIONS

General Precautions

Discontinuation of Treatment With Venlafaxine

Discontinuation symptoms have been systematically evaluated in patients taking venlafaxine. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible.

Anxiety and Insomnia

Treatment-emergent anxiety, nervousness, and insomnia were more commonly reported for venlafaxine treated patients compared to placebo-treated patients.

Changes in Weight

Adult Patients

A dose-dependent weight loss was noted in patients treated with venlafaxine for several weeks. A loss of 5% or more of body weight occurred in 6% of patients treated with venlafaxine compared with 1% of patients treated with placebo and 3% of patients treated with another antidepressant.

Pediatric Patients

Weight loss has been observed in pediatric patients (ages 6 to 17) receiving venlafaxine hydrochloride extended-release capsules.

Changes In Height

Pediatric Patients

During the eight-week placebo-controlled GAD studies, venlafaxine hydrochloride extended-release capsule-treated patients (ages 6 to 17) grew an average of 0.3 cm (n = 122), while placebo-treated patients grew an average of 1.0 cm (n = 132).

Changes In Appetite

Adult Patients

Treatment-emergent anorexia was more commonly reported for venlafaxine-treated (11%) than placebotreated patients (2%)

Pediatric Patients

Decreased appetite has been observed in pediatric patients receiving venlafaxine hydrochloride extended-release capsules

Seizures

During premarketing testing, seizures were reported in 0.26% (8/3082) of venlafaxine-treated patients. Most seizures (5 of 8) occurred in patients receiving doses of 150 mg/day or less.

Abnormal Bleeding

SSRIs and SNRIs, including venlafaxine may increase the risk of bleeding events.

Interstitial Lung Disease And Eosinophilic Pneumonia

Interstitial lung disease and eosinophilic pneumonia associated with venlafaxine therapy have been rarely reported

Use In Patients With Concomitant Illness

Clinical experience with venlafaxine in patients with concomitant systemic illness is limited. Caution is advised in administering venlafaxine to patients with diseases or conditions that could affect hemodynamic responses or metabolism.

CONTRAINDICATIONS

Hypersensitivity to venlafaxine hydrochloride or to any excipients in the formulation.

The use of MAOIs intended to treat psychiatric disorders with Venlafaxine or within 7 days of stopping treatment with venlafaxine is contraindicated because of an increased risk of serotonin syndrome.

OVERDOSAGE

Overdose with venlafaxine has occurred predominantly in combination with alcohol and/or other drugs. The most commonly reported events in over dosage 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), ventricular tachycardia, bradycardia, hypotension, rhabdomyolysis, vertigo, liver necrosis, serotonin syndrome.

Management Of Over dosage

Treatment should consist of those general measures employed in the management of over dosage with any antidepressant.

Ensure an adequate airway, oxygenation, and ventilation. Monitor cardiac rhythm and vital signs. General supportive and symptomatic measures are also recommended. 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.

STORAGE

Store below 30°C.

Protect from light, heat and moisture.

Keep out of the reach of children.

PRESENTATION

Faxine (Venlafaxine as HCl) 50mg Tablets:

Pack of 2 X 10's in Alu-PVC blister

Faxine-SR (Venlafaxine as HCl) 75mg Capsules:

Pack of of 2 X 7's in Alu-Alu blister.

خوراک اور ہدایات:

ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

دوا کو **30** درجہ سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔

روشنی، گرمی اور نمی سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔

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