LOXE
(Duloxetine)
20mg
30mg
60mg
Delayed-Release
Capsules U.S.P.

لوکس
۲۰ ملی گرام ۳۰ ملی گرام ۶۰ ملی گرام
(ڈیولاکساٹین)
کیپسولز یو۔ایس۔پی۔

QUALITATIVE AND QUANTITATIVE COMPOSITION

Loxe Capsule 20mg U.S.P.
Each capsule contains:
Duloxetine HCl enteric-coated pellets
equivalent to Duloxetine.....20mg

Loxe Capsule 30mg U.S.P.
Each capsule contains:
Duloxetine HCl enteric-coated pellets
equivalent to Duloxetine.....30mg

Loxe Capsule 60mg U.S.P.
Each capsule contains:
Duloxetine HCl enteric-coated pellets
equivalent to Duloxetine.....60mg

WARNING: SUICIDAL THOUGHTS AND BEHAVIORS

- Increased risk of suicidal thinking and behavior in children, adolescents, and young adults taking antidepressants.
- Monitor for worsening and emergence of suicidal thoughts and behaviors.

DESCRIPTION

Duloxetine hydrochloride is a selective serotonin and norepinephrine re-uptake inhibitor (SSNRI) for oral administration. Its chemical designation is (+)-(S)-N-methyl-γ-(1-naphthyloxy)2-thiophenepropylamine hydrochloride.

CLINICAL PHARMACOLOGY

Mechanism of Action: Potentiation of serotonergic and noradrenergic activity in the CNS.
Pharmacodynamics: Duloxetine is a potent inhibitor of neuronal serotonin and norepinephrine reuptake and a less potent inhibitor of dopamine re-uptake.
Pharmacokinetics: Duloxetine has an elimination half-life of about 12 hours (range 8 to 17 hours) and its pharmacokinetics are dose proportional over the therapeutic range. Steady-state plasma concentrations are typically achieved after 3 days of dosing. Elimination of duloxetine is mainly through hepatic metabolism involving two P450 isozymes, CYP1A2 and CYP2D6.
Absorption and Distribution: Orally administered duloxetine hydrochloride is well absorbed. Food does not affect the Cmax of duloxetine, but delays the time to reach peak concentration from 6 to 10 hours and it marginally decreases the extent of absorption (AUC) by about 10%. There is a 3 hour delay in absorption and a one-third increase in apparent clearance of duloxetine after an evening dose as compared to a morning dose. The apparent volume of distribution averages about 1640L. Plasma protein binding of duloxetine is not affected by renal or hepatic impairment.
Metabolism and Elimination: The major biotransformation pathways for duloxetine involve oxidation of the naphthyl ring followed by conjugation and further oxidation. Metabolites found in plasma include 4-hydroxy duloxetine glucuronide and 5- hydroxy, 6-methoxy duloxetine sulfate.
Children and Adolescents (ages 7 to 17 years): The average steady-state duloxetine concentration was approximately 30% lower in the pediatric population (children and adolescents) relative to the adults.

INDICATIONS AND USAGE

Loxe capsule is a serotonin and norepinephrine reuptake inhibitor (SNRI) indicated for:

- Major Depressive Disorder (MDD)
- Generalized Anxiety Disorder (GAD)
- Diabetic Peripheral Neuropathic Pain (DPNP)
- Fibromyalgia (FM)
- Chronic Musculoskeletal Pain

CONTRAINDICATIONS:

Monoamine Oxidase Inhibitors (MAOIs): The use of MAOIs intended to treat psychiatric disorders with Loxe or within 5 days of stopping treatment with Loxe is contraindicated because of an increased risk of serotonin syndrome. The use of Loxe within 14 days of stopping an MAOI intended to treat psychiatric disorders is also contraindicated. Starting Loxe in a patient who is being treated with MAOIs such as linezolid or intravenous methylene blue is also contraindicated because of an increased risk of serotonin syndrome. IN **TERACTIONS:** Both CYP1A2 and CYP2D6 are responsible for duloxetine metabolism. Inhibitors of CYP1A2: When duloxetine 60 mg was co-administered with fluvoxamine 100 mg, a potent CYP1A2 inhibitor, duloxetine AUC was increased approximately 6-fold, the Cmax was increased about 2.5-fold, and duloxetine t1/2 was increased approximately 3-fold. Inhibitors of CYP2D6: Concomitant use of duloxetine (40 mg once daily) with paroxetine (20 mg once daily) increased the concentration of duloxetine AUC by about 60%, and greater degrees of inhibition are expected with higher doses of paroxetine.

Drugs Metabolized by CYP2D6: Duloxetine is a moderate inhibitor of CYP2D6. When duloxetine was administered (at a dose of 60 mg twice daily) in conjunction with a single 50mg dose of desipramine, a CYP2D6 substrate, the AUC of desipramine increased 3-fold.

Dual Inhibition of CYP1A2 and CYP2D6: Concomitant administration of duloxetine 40 mg twice daily with fluvoxamine 100 mg, a potent CYP1A2 inhibitor, to CYP2D6 poor metabolizer subjects (n=14) resulted in a 6-fold increase in duloxetine AUC and Cmax.

Co-administration of Loxe: Co-administration of Loxe is prohibited with drugs that interfere with hemostasis (e.g., NSAIDs, Aspirin, and Warfarin), drugs that affect gastric acidity, alcohol, and use with caution incase of CNS drugs. Drugs Metabolized by CYP2C19: Duloxetine does not inhibit CYP2C19 activity at therapeutic concentrations.

Drugs Highly Bound to Plasma Protein: A highly protein bound drug may cause increased free concentrations of the other drug, potentially resulting in adverse reactions. USE

IN SPECIFIC POPULATION

Pregnancy Category C: There are no adequate studies of Duloxetine administration in pregnant women.

Fetal/Neonatal Adverse Reaction: Respiratory distress, cyanosis, apnea, seizures, temperature instability, feeding difficulty, vomiting, hypoglycemia, hypotonia, hypertonia, hyperreflexia, tremor, jitteriness, irritability, and constant crying.

Nursing Mothers: Duloxetine is present in human milk. Exercise caution when Loxe is administered to a nursing woman. The presence of Duloxetine metabolites in breast milk was not examined.

Pediatric Use: Generalized Anxiety Disorder The safety and effectiveness in pediatric patients less than 7 years of age have not been established. Major Depressive Disorder Nausea, headache, decreased weight, and abdominal pain occur. Decreased appetite and weight loss have been observed in association with the use of SSRIs and SNRIs. Perform regular monitoring of weight and growth in children and adolescents treated with an SNRI such as Duloxetine.

Geriatric Use: Loxe have been associated with cases of clinically significant

hyponatremia in elderly patients, who may be at greater risk for this adverse event. Dosage adjustment based on the age of the patient is not necessary.
Gender: Duloxetine's half life is similar in men and women. Dosage adjustment based on gender is not necessary.
Smoking Status: Duloxetine bioavailability (AUC) appears to be reduced by about one-third in smokers. Dosage modifications are not recommended for smokers. Hepatic Impairment: Patients face decreased duloxetine metabolism and elimination. Avoid use in patients with chronic liver disease or cirrhosis.
Severe Renal Impairment: Mild to moderate degrees of renal impairment (estimated CrCl 30-80mL/min) have no significant effect on duloxetine apparent clearance. Avoid use in patients with severe renal impairment, GFR <30 mL/min.

PRECAUTIONS:

Hepatotoxicity: Hepatitis with abdominal pain, hepatomegaly, and elevation of transaminase levels occur. Loxe should be discontinued in patients who develop jaundice. Cholestatic jaundice with minimal elevation of transaminase levels also occur. Elevated transaminases, bilirubin, and alkaline phosphatase have occurred in patients with chronic liver disease or cirrhosis. Orthostatic Hypotension, Falls and Syncope: Orthostatic hypotension, falls and syncope have been reported with therapeutic doses of Duloxetine, occur within the first week of therapy but can occur at any time during Loxe treatment, particularly after dose increases. Serotonin Syndrome: It occurs with SNRIs and SSRIs, including Loxe, alone but particularly with concomitant use of other serotonergic drugs.
Abnormal Bleeding: SSRIs and SNRIs, including Duloxetine, may increase the risk of bleeding events.
Severe Skin Reactions: Erythema multiforme and Stevens Johnson Syndrome (SJS), can occur with Duloxetine.
Activation of Mania/Hypomania: In adult patients with major depressive disorder, activation of mania or hypomania was reported. Angle Closure Glaucoma: The pupillary dilation that occurs following use of many antidepressant drugs including Loxe may trigger an angle closure attack in a patient with anatomically narrow angles who does not have a patent iridectomy.
Seizures: Loxe should be prescribed with care in patients with a history of a seizure disorder.
Effect on Blood Pressure: Duloxetine treatment was associated with mean increases of 0.5 mm Hg in systolic blood pressure and 0.8 mm Hg in diastolic blood pressure. Alcohol: Loxe concomitantly with heavy alcohol intake may be associated with severe liver injury. CNS Acting Drugs: Given the primary CNS effects of Loxe, it should be used with caution when it is taken in combination with or substituted for other centrally acting drugs, including those with a similar mechanism of action.
Hyponatremia: Signs and symptoms of hyponatremia include headache, difficulty concentrating, memory impairment, confusion, weakness, and unsteadiness. More severe and/or acute cases have been associated with hallucination, syncope, seizure, coma, respiratory arrest, and death.
Use in Patients with Concomitant Illness: Clinical experience with Duloxetine in patients with concomitant systemic illnesses is limited. In extremely acidic conditions, Duloxetine unprotected by the enteric coating, may undergo hydrolysis to form naphthol. Caution is advised in using Loxe in patients with conditions that may slow gastric emptying (some diabetics). Glycemic Control in Patients with Diabetes: Treatment worsens glycemic control in some patients with diabetes.
Urinary Hesitation and Retention: Loxe is in a class of drugs known to affect urethral resistance.

ADVERSE REACTIONS

Most common adverse reactions (≥5% and at least twice the incidence of placebo patients): nausea, dry mouth, somnolence, fatigue, constipation,

decreased appetite, and hyperhidrosis.

DOSAGE AND ADMINISTRATION

Take Loxe once daily, with or without food. Swallow Loxe whole; do not crush or chew, do not open capsule.

INDICATION	STARTING DOSE	TARGET DOSE	MAXIMUM DOSE
MDD	40mg/day to 60mg/day	**AcuteTreatment:** 40mg/day(20mg	120mg/day
		twice daily) to 60mg/day	
		(once daily or as 30mg twice daily);	
		Maintenance Treatment: 60mg/day	
GAD			
Adults	60mg/day	60mg/day(once daily)	120mg/day
Elderly	30mg/day	60mg/day(once daily)	120mg/day
Children and Adolescents (7to17years of age)	30mg/day	30 to 60mg/day (once daily)	120mg/day
DPNP	60mg/day	60mg/day (once daily)	60mg/day
FM	30mg/day	60mg/day (once daily)	60mg/day
Chronic Musculoskeletal pain	30mg/day	60mg/day (once daily)	60mg/day

Some patients may benefit from starting at 30 mg once daily. There is no evidence that doses greater than 60 mg/day confers additional benefit, while some adverse reactions were observed to be dose-dependent.

Discontinuing Loxe: Dizziness, headache, nausea, diarrhea, paresthesia, irritability, vomiting, insomnia, anxiety, hyperhidrosis, and fatigue may occur. A gradual reduction in dosage rather than abrupt cessation is recommended whenever possible.

Overdosage: Fatal outcomes have been reported for acute overdoses. Signs and symptoms of overdose (duloxetine alone or with mixed drugs) included somnolence, coma, serotonin syndrome, seizures, syncope, tachycardia, hypotension, hypertension, and vomiting.

Management of Overdose: There is no specific antidote to Loxe. An adequate airway, oxygenation, and ventilation, 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, Activated charcoal maybe used. Forced diuresis, dialysis, hemoperfusion, and exchange transfusion are unlikely to be beneficial. The possibility of multiple drug involvement should be considered. Incase of taken Loxe and might ingest excessive quantities of a TCA, 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.

Missed dose: If it is almost time for the next dose, skip the missed dose and take the next dose at the regular time. Do not take two doses of Loxe at the same time.

DOSAGE

As directed by the physician.

INSTRUCTIONS

Store at 25°C, excursions permitted to 15°C-30°C. Protect from sunlight and Moisture.

PRESENTATION

Loxe (Duloxetine) Delayed-Release Capsules U.S.P. 20mg are available in ALU/PVC blister pack of 14's.

Loxe (Duloxetine) Delayed-Release Capsules U.S.P. 30mg are available in ALU/PVC blister pack of 14's.

Loxe (Duloxetine) Delayed-Release Capsules U.S.P. 60mg are available in ALU/PVC blister pack of 14's.

علامات/طریقہ استعمال: **لوکس** کیپسولز مندرجہ ذیل علامات میں تجویز کردہ ہے۔

• میجر ڈپریسیوڈس آرڈر • اضطرابی بیماری • ذیابیطس سے منسلک اعصابی درد • فبرومیئلجیا • دائمی پٹھوں کا درد

لوکس کیپسول دن میں ایک مرتبہ کھانے کے ساتھ یا بغیر کھانے کے لی جاسکتی ہے۔مختلف امراض کے لحاظ سے خوراک ڈاکٹر کی ہدایت کے مطابق تجویز کردہ ہے۔
لوکس کیپسول کو ثابت نگلنا ہے۔چبانے،توڑنے اور کھولنے سے گریز کریں۔

مضر اثرات: • متلی • تھکن • قبض • بھوک میں کمی • خشک منہ • غنودگی • پسینہ زیادہ آنا • بلڈ پریشر کا کم ہوجانا • جسم میں سوڈیم کی مقدار میں کمی
• خون کے منجمد ہونے کے دورانیہ میں اضافہ

احتیاطی تدابیر: • جلد اور جگر کے امراض ہونے کا خدشہ ہے۔

خوراک: معالج کی ہدایت کے مطابق استعمال کریں۔

ہدایات: ۲۵ ڈگری سینٹی گریڈ پر رکھیں محفوظ رکھنے کی حد ۱۵ سے ۳۰ ڈگری سینٹی گریڈ ہے۔سورج کی روشنی اور نمی سے محفوظ رکھیں۔تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔

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