Loxetine®

Duloxetine

Description

Loxetine® is a preparation of Duloxetine Hydrochloride which is a potent inhibitor of neuronal serotonin and norepinephrine reuptake and a less potent inhibitor of dopamine reuptake. Duloxetine has no significant affinity for dopaminergic, adrenergic, cholinergic, histaminergic, opioid, glutamate, and GABA receptors *in vitro*. Duloxetine does not inhibit monoamine oxidase (MAO). The pain inhibitory action of Duloxetine is believed to be a result of potentiation of descending inhibitory pain pathways within the central nervous system.

Indication and usage

Loxetine® is indicated for the treatment of

- Major Depressive Disorder (MDD)
- Generalized Anxiety Disorder (GAD)
- Diabetic Peripheral Neuropathy
- Fibromyalgia
- Chronic Musculoskeletal Pain
- Stress Urinary Incontinence

Dosage and administration

Major Depressive Disorder: Loxetine® should be administered at a total dose of 40 mg/day (given as 20 mg twice daily) to 60 mg/day (given either once daily or as 30 mg twice daily). For some patients, it may be desirable to start at 30 mg once daily for 1 week, to allow patients to adjust to the medication before increasing to 60 mg once daily.

Generalized Anxiety Disorder:

Adult: For most patients, the recommended starting dose of Loxetine® is 60 mg once daily. For some patients, it may be desirable to start at 30 mg once daily for 1 week, to allow patients to adjust to the medication before increasing to 60 mg once daily.

Elderly: The recommended starting dose of Loxetine® is 30 mg once daily for 2 weeks before considering an increase to the target dose of 60 mg. Thereafter, patients may benefit from doses above 60 mg once daily.

Children and Adolescents (7 to 17 years of age): The recommended starting dose of Loxetine® is 30 mg once daily for 2 weeks before considering an increase to 60 mg. The recommended dose range is 30 to 60 mg once daily.

Diabetic Peripheral Neuropathy: **The recommended starting dose of Loxetine® is 60 mg once daily. Since diabetes is frequently complicated by renal disease, a lower starting dose and gradual increase in dose should be considered for patients with renal impairment.**

Fibromyalgia: The recommended starting dose of Loxetine® is 60 mg once daily. Treatment should be started at 30 mg once daily for 1 week to allow patients to adjust to the medication before increasing to 60 mg once daily.

Chronic Musculoskeletal Pain: The recommended starting dose of Loxetine® is 60 mg once daily. Dosing may be started at 30 mg for 1 week, to allow patients to adjust to the medication before increasing to 60 mg once daily.

Stress Urinary Incontinence: The recommended starting dose of Loxetine® is 80mg once daily (40mg twice daily). If patients continue to experience adverse effects beyond the initial four weeks of treatment, the dosage may be reduced to 20 mg twice daily.

Elderly*:* No dosage adjustment is recommended for elderly patients solely on the basis of age. However, caution should be exercised when treating the elderly, especially with Duloxetine 120 mg per day for major depressive disorder or generalized anxiety disorder.
Hepatic Impairment*:* Avoid use in patients with chronic liver disease or cirrhosis.

Renal Impairment*:* No dosage adjustment is necessary for patients with mild or moderate renal dysfunction (creatinine clearance 30 to 80 ml/min). Duloxetine must not be used in patients with severe renal impairment (creatinine clearance <30 ml/min).

Pediatric population*:* The safety and effectiveness of Duloxetine in pediatric patients less than 7 years of age have not been established.

Use in pregnancy and lactation:
Pregnancy: Duloxetine is pregnancy category C. There are no adequate data and well-controlled studies on the use of Duloxetine in pregnant women. Duloxetine should be used in pregnancy only if the potential benefit justifies the potential risk to the fetus.
Lactation: As the safety of Duloxetine in infants is not known, the use of Duloxetine while breast-feeding is not recommended.

Side effects
The most common side effects are nausea, vomiting, dyspepsia, constipation, diarrhea, abdominal pain, weight changes, decreased appetite, flatulence, dry mouth, palpitation, hot flush, insomnia, abnormal dreams, paraesthesia, drowsiness, anxiety, headache, dizziness, fatigue, weakness, tremor, nervousness, anorexia, sexual dysfunction, sweating, pruritus, visual disturbances; less commonly gastritis, halitosis, hepatitis, dysphagia, tachycardia, hypertension, postural hypo-tension, syncope, raised cholesterol, vertigo, taste disturbance, cold extremities, impaired temperature regulation, impaired attention, movement disorders.

Contraindication
Duloxetine is contraindicated in patients with a known hypersensitivity to this drug or any of the ingredients. Concomitant use of Duloxetine with non-selective, irreversible monoamine oxidase inhibitors (MAOIs) is contraindicated. Use of Duloxetine in patients with liver disease, severe renal impairment, uncontrolled hypertension that could expose them to a potential risk of hypertensive crisis is contraindicated.

Precautions
Duloxetine should be used with caution in patients with a history of mania or a diagnosis of bipolar disorder, and/or seizures. Caution should be used when prescribing Duloxetine to patients with increased intraocular pressure or those at risk of acute narrow-angle glaucoma. Duloxetine should be used with caution in patients whose conditions could be compromised by an increased heart rate or by an increase in blood pressure. In patients with uncontrolled hypertension, Duloxetine should not be initiated.

Drug interactions
Both CYP1A2 and CYP2D6 are responsible for Duloxetine metabolism. Concomitant use of Duloxetine with potent inhibitors of CYP1A2 is likely to result in higher concentrations of Duloxetine. Fluvoxamine (100 mg once daily), a potent inhibitor of CYP1A2, decreased the

apparent plasma clearance of Duloxetine by about 77% and increased AUC to 6-fold. The risk of using Duloxetine in combination with other CNS-active medicinal products has not been systematically evaluated. Consequently, caution is advised when Duloxetine is taken in combination with other centrally-acting medicinal products or substances, including alcohol and sedative medicinal products (e.g., benzodiazepines, morphinomimetics, antipsychotics, phenobarbital, sedative antihistamines).

Overdose
There is limited clinical experience with Duloxetine overdose in humans. There is no specific antidote to Duloxetine. 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.

Pharmaceutical precautions
Store in a cool (between 15^0C to 30^0C) and dry place. Protect from light.

Presentation
Loxetine® 20 tablet: Each delayed release tablet contains Duloxetine 20 mg as Hydrochloride USP.
Loxetine® 30 tablet: Each delayed release tablet contains Duloxetine 30 mg as Hydrochloride USP.

Package quantities
Loxetine® 20 tablet: Carton of 30 tablets in blister pack.

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