SENOBIT®

सेनोविट

1. Product Name
SENOBIT® 20: Duloxetine Delayed Release Capsules USP
SENOBIT® 30: Duloxetine Delayed Release Capsules USP
SENOBIT® 60: Duloxetine Delayed Release Capsules USP

2. Name and Strength of Active Ingredient(s)
SENOBIT® 20
Each hard gelatin capsule contains:
Duloxetine pellets equivalent to Duloxetine 20 mg
SENOBIT® 30
Each hard gelatin capsule contains:
Duloxetine pellets equivalent to Duloxetine 30 mg
SENOBIT® 60
Each hard gelatin capsule contains:
Duloxetine pellets equivalent to Duloxetine 60 mg

3. Product Description
SENOBIT is Duloxetine, an antidepressant medicine (a medicine used to treat depression and anxiety). Duloxetine works by restoring the balance of serotonin and norepinephrine in the brain. It improves mood, sleep, appetite, energy level and decreases nervousness.

4. Pharmacodynamics & Pharmacokinetics
Pharmacodynamics:
The central pain inhibitory and anxiolytic actions of duloxetine in humans are believed to be related to its potentiation of serotonergic and noradrenergic activity in the CNS. It is an inhibitor of neuronal serotonin and norepinephrine reuptake and a less potent inhibitor of dopamine reuptake. It has no significant affinity for dopaminergic, adrenergic, cholinergic, histaminergic, opioid, glutamate, and GABA receptors *in vitro*. The pain inhibitory action of duloxetine is believed to be a result of potentiation of descending inhibitory pain pathways within the central nervous system.

Pharmacokinetics
Absorption:
Duloxetine is well absorbed after oral administration, with a C_{max} occurring 6 hours post-dose. The absolute oral bioavailability of duloxetine ranged from 32% to 80% (mean of 50%). Food delays the time to reach the peak concentration from 6 to 10 hours and it marginally decreases the extent of absorption (approximately 11%). These changes do not have any clinical significance.
Distribution:
Duloxetine is approximately 96% bound to human plasma proteins. It binds to both albumin and alpha1-acid glycoprotein. Protein binding is not affected by renal or hepatic impairment.
Metabolism:
Duloxetine is extensively metabolised and the metabolites are excreted principally in urine. Both cytochromes P450-2D6 and 1A2 catalyse the formation of the two major metabolites, glucuronide conjugate of 4-hydroxy duloxetine and sulfate conjugate of 5-hydroxy, 6-methoxy duloxetine. Based upon in vitro studies, the circulating metabolites of duloxetine are considered pharmacologically inactive.
Excretion:
The elimination half-life of duloxetine ranges from 8 to 17 hours (mean of 12 hours). After an oral dose, the apparent plasma clearance of duloxetine ranges from 33 to 261 l/hr (mean 101 l/hr).

5. Indications:
- Treatment of Major Depressive Disorder
- Treatment of Diabetic Peripheral Neuropathic Pain
- Treatment of Generalized Anxiety Disorder
- Treatment of Urinary Incontinence

6. Recommended Dose and Administration
Major Depressive Disorder:
The starting and recommended maintenance dose is 60 mg once daily with or without food. Dosages above 60 mg once daily, up to a maximum dose of 120 mg per day have been evaluated from a safety perspective in clinical trials. Therapeutic response is usually seen after 2-4 weeks of treatment. In patients responding to Duloxetine, and with a history of repeated episodes of major depression, further long-term treatment at a dose of 60 to 120 mg/day could be considered.
Generalised Anxiety Disorder:
The recommended starting dose in patients with Generalised Anxiety Disorder is 30 mg once daily with or without food. In patients with insufficient response the dose should be increased to 60 mg, which is the usual maintenance dose in most patients. In patients with co-morbid Major Depressive Disorder, the starting and maintenance dose is 60 mg once daily. In patients with insufficient response to 60 mg, escalation up to 90 mg or 120 mg may therefore be considered. Doses up to 120 mg per day have been shown to be efficacious and have been evaluated from a safety perspective in clinical trials. Dose escalation should be based upon clinical response and tolerability.
Diabetic Peripheral Neuropathic Pain:
The starting and recommended maintenance dose is 60 mg daily with or without food. Dosages above 60 mg once daily, up to a maximum dose of 120 mg per day administered in evenly divided doses, have been evaluated from a safety perspective in clinical trials. Some patients that respond insufficiently to 60 mg may benefit from a higher dose.
Stress Urinary Incontinence (SUI):
The recommended dose is 40 mg twice daily without regard to meals. After 2-4 weeks of treatment, patients should be re-assessed in order to evaluate the benefit and tolerability of the therapy. Some patients may benefit from starting treatment at a dose of 20 mg twice daily for two weeks before increasing to the recommended dose of 40 mg twice daily.
Hepatic Impairment:
Duloxetine must not be used in patients with liver disease resulting in hepatic impairment.
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).

7. Contraindications

Contraindicated in patients with hypersensitivity to the active substance or to any of the excipients; concomitant use with non-selective, irreversible monoamine oxidase inhibitors (MAOIs) and combined use with fluvoxamine, ciprofloxacin or enoxacin (i.e. potent CYP1A2 inhibitors).

8. Special Populations

Elderly:

No dosage adjustment is recommended for elderly patients solely on the basis of age. However, as with any medicine, caution should be exercised when treating the elderly.

Paediatric population:

Duloxetine should not be used in children and adolescents under the age of 18 years for the treatment of Major Depressive Disorder because of safety and efficacy concerns.

Pregnancy & Lactation:

Pregnancy Category C. Duloxetine is very weakly excreted in human milk. The safety of duloxetine in infants is not known, so decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

9. Warnings and Precautions

- Should be used with caution in patients with a history of mania or a diagnosis of bipolar disorder, and/or seizures.
- Mydriasis has been reported in association with duloxetine, therefore, caution should be used when prescribing duloxetine to patients with increased intraocular pressure or those at risk of acute narrow-angle glaucoma
- Duloxetine has been associated with an increase in blood pressure and clinically significant hypertension in some patients. In patients with known hypertension and/or other cardiac disease, blood pressure monitoring is recommended, especially during the first month of treatment.

10. Drug-Drug Interactions

- Due to risk of serotonin syndrome, duloxetine should not be used in combination with non-selective, irreversible monoamine oxidase inhibitors (MAOIs) or within at least 14 days of discontinuing treatment with an MAOI.
- Because CYP1A2 is involved in duloxetine metabolism, its concomitant use with potent inhibitors of CYP1A2 is likely to result in higher concentrations of duloxetine.
- In rare cases, serotonin syndrome has been reported in patients using SSRIs/SNRIs concomitantly with serotonergic agents.
- Caution is advised when duloxetine is taken in combination with other centrally-acting medicinal products or substances, including alcohol and sedative medicinal products.

11. Undesirable Effects

Some of the common adverse reactions include:

- Nausea, headache, dry mouth, somnolence, decreased appetite, dizziness.
- Lethargy, tremor, paresthesia, blurred vision, palpitation

12. Storage Condition

Protect from direct sunlight and moisture. Store SENOBIT below 30 ºC at cool and dry place but not in refrigerator. Keep the medication away from children and pets.

13. Dosage Forms and Packaging Available

SENOBIT® 20 Capsules: Each Box contains 10 Capsules X 10 Blisters
SENOBIT® 30 Capsules: Each Box contains 10 Capsules X 10 Blisters
SENOBIT® 60 Capsules: Each Box contains 10 Capsules X 10 Blisters

Manufactured by:
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