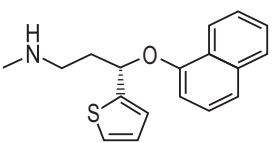
DTIN
(Duloxetine)

30mg CAPSULE

DTIN (Duloxetine) is a selective serotonin and norepinephrine reuptake inhibitor (SSNRI) for oral administration. Its chemical designation is (+)-(S)-N-methyl-•-(1-naphthyloxy)-2-thiophenepropylamine hydrochloride. The empirical formula is $C_{18}H_{19}NOS$•HCl.



COMPOSITION:
Each hard gelatin capsule contains:
Enteric coated pellets of Duloxetine Hcl
Equivalent to Duloxetine USP .....30mg.

CLINICAL PHARMACOLOGY:

Pharmacokinetics

Absorption

Orally administered Duloxetine hydrochloride is well absorbed. Maximal plasmaconcentrations (Cmax) of Duloxetine occurring 6 hours post dose. Food does not affect the Cmax of Duloxetine, but delays the time to reach peak concentration from 6 to 10hours and it marginally decreases the extent of absorption (AUC) by about 10%. The absolute oral bioavailability of Duloxetine ranges from 32% to 80% (mean of 50%).

Distribution

Duloxetine is highly bound (>90%) to proteins in blood plasma, binding primarily to albumin and 1-acid glycoprotein. Plasma protein binding of Duloxetine is not affected by renal or hepatic impairment.

Metabolism

Duloxetine undergoes extensive metabolism. The 2 major metabolites found in plasma and urine are the glucuronide conjugate of 4-hydroxy Duloxetine, and the sulfate conjugate of 5-hydroxy, 6-methoxy Duloxetine. Both CYP2D6 and CYP1A2 catalyze the formation of the initial oxidation steps to form 4, 5 and 6-hydroxy Duloxetine. The metabolites circulating in plasma are in the conjugated form and are not pharmacologically active.

Elimination

Duloxetine has an elimination half-life of about 12 hours (range 8 to 17 hours) and their pharmacokinetics is 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.

Pharmacodynamics

Mechanism of Action

Duloxetine is a selective serotonin and noradrenaline reuptake inhibitor, and weakly inhibits dopamine uptake with no significant affinity for histaminergic, dopaminergic,cholinergic and adrenergic receptors.Although the exact mechanisms of the central pain inhibitory and anxiolytic actions of Duloxetine in humans are unknown, these actions are believed to be related to its potentiation of serotonergic and noradrenergic activity in the CNS.

INDICATIONS AND USAGE:
DTIN 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:
Duloxetine must not be used in patients hypersensitive to Duloxetine or any other component of product.

PRECAUTIONS:

SUICIDAL THOUGHTS AND BEHAVIORS

Antidepressants increase the risk of suicidal thoughts and behavior in children, adolescents and young adults in short-term studies. These studies did not show an increase in the risk of suicidal thoughts and behavior with antidepressant use in patients over age 24; there was a reduction in risk with antidepressant use in patients aged 65 and older. In patients of all ages who have started on antidepressant therapy, monitor closely for worsening and for emergence of suicidal thoughts and behaviors. Advise families and caregivers of the need for close observation and communication with the prescriber.

SIDE EFFECTS

Nausea
Dizziness
Sweating
Headache
Fatigue
Seizure
Chronic Pain due to Osteoarthritis
Chronic Low Back Pain

DRUG INTERACTIONS:

Monoamine Oxidase inhibitors (MAOIs): Due to the risk of serotonin syndrome, Duloxetine should not be used in combination with non-selective irreversible monoamine Oxidase inhibitors (MAOIs) or within at least 14 day of discontinuing treatment with an MAOI CNS medicinal products: Caution is advised when Duloxetine is takens in combination with other centrally acting medicinal products or substances including alcohol and sedative medicinal products (e.g. benzodiazepines, morphinomimetics, antipsychotics,Phenobarbital, sedative antihistamines) Serotonin syndrome: Patients using SSRIs/SNRIs concomitantly with serotonergic agents. Caution is advisable if Duloxetine is used concomitantly with serotonergic agents like SSRIs, SNRIs, tricyclic antidepressants like clomipramine or amitriptyline, MAOIs like moclobemide or Linezolid, St John's wort (Hypericum perforatum) or triptans,tramadol,pethidine and tryptophan.

Effect of Duloxetine on other medicinal products:

Medicinal products metabolized by CYP1A2:The pharmacokinetics of theophylline, a CYP1A2 substrate, were not significantly affected by co-administration with Duloxetine(60 mg twice daily). Anticoagulants and antiplatelet agents; Caution should be exercised when Duloxetine is combined with oral anticoagulants or antiplatelet agents due to a potential increased risk of bleeding attributable to a pharmacodynamic interaction.

Indication	Starting Dose	Target Dose	Maximum Dose
Major Depressive Disorder	40mg/day	60mg/day	Acute Treatment
Generalized Anxiety Disorder			
Adults	60mg/day	60mg/day	120mg/day
Elderly	30mg/day	60mg/day	120mg/day
Children and Adolescents (7 to 17 years of age)	30mg/day	60mg/day	120mg/day
Diabetic Peripheral	Neuropathic pain	60mg/day	60mg/day (once daily)
Fibromyalgia	30mg/day	60mg/day	60mg/day
Chronic Musculoskeletal pain	30mg/day	60mg/day	60mg/day

OR

As directed by the physician

STORAGE & INSTRUCTIONS:

Keep out of the reach of children & Store below 30°C.
Protect from sunlight & moisture
Improper storage may deteriorate the medicine
Do not use this medicine after the expiry date which is stated on the blister.

STABILITY:

See expiry on pack.

PRESENTATION:

DTIN 30mg capsule in pack of 10's.

Manufactured by :
PHARMA LORD
PHARMA LORD (PVT.) LIMITED | 12km, Lahore Road, Layyah. Pakistan
www.pharma-lord.com