PROLONG

Dapoxetine Tablet

Composition:
PROLONG 30 : Each film coated tablet contains Dapoxetine Hydrochloride INN equivalent to Dapoxetine 30 mg.
PROLONG 60 : Each film coated tablet contains Dapoxetine Hydrochloride INN equivalent to Dapoxetine 60 mg.

Pharmacology:
The mechanism of action of Dapoxetine in premature ejaculation is presumed to be linked to the inhibition of neuronal reuptake of serotonin and the subsequent potentiation of the neurotransmitter's action at pre-and post synaptic receptors. Human ejaculation is primarily mediated by the sympathetic nervous system. The ejaculatory pathway originates from a spinal reflex centre, mediated by the brain stem, which is influenced initially by a number of nuclei in the brain (medial preoptic and paraventricular nuclei).
Dapoxetine is rapidly absorbed with maximum plasma concentrations (C_{max}) occurring approximately 1-2 hours after tablet intake. The absolute bioavailability is 42%. More than 99% of Dapoxetine is bound in-vitro to human serum proteins. The active metabolite Desmethyl dapoxetine (DED) is 98.5% protein bound. Dapoxetine appears to have a rapid distribution with a mean steady state volume of distribution of 162 L.
Dapoxetine is extensively metabolized to multiple metabolites primarily through the following biotransformational pathways: N-oxidation, N-demethylation, Naphthyl hydroxylation, Glucuronidation and Sulfation. There was evidence of presystemic first-pass metabolism after oral administration. The metabolites of the Dapoxetine were primarilly eliminated in urine as conjugates. Dapoxetine has a rapid elimitaion and the terminal half life is approximately 19 hours.

Indication:
Dapoxetine Hydrochloride tablet is indicated for the treatment of Premature Ejaculation in men 18 to 64 years of age.

Dosage and Administration :
For Premature Ejaculation:
Adult men (18 to 64 years of age): The recommended starting dose for all patients is 30 mg, taken as needed approximately 1 to 3 hours prior to sexual activity. The maximum recommended dosing frequency is once every 24 hours. If the effect of 30 mg is insufficient and the side effects are acceptable, the dose may be increased to the maximum recommended dose of 60 mg. Dapoxetine may be taken with or without food.

Children and adolescents:
Dapoxetine should not be used in individuals below 18 years of age. **Elderly (age 65 years and over):** Safety and efficacy of Dapoxetine have not been established in patients age 65 years and over as limited data are available in this population.

Patients with renal impairment:
Caution is advised in patients with mild or moderate renal impairment. Dapoxetine is not recommended for use in patients with severe renal impairment.

Patients with hepatic impairment:
Dapoxetine is contraindicated in patients with moderate and severe hepatic impairment.

Pregnancy : Dapoxetine is not indicated for use by women.

Warnings and Precautions:

General:
Use with recreational drugs: Patients should be advised not to use Dapoxetine in combination with recreational drugs. Recreational drugs with serotonergic activity such as ketamine, methylenedioxymethamphetamine (MDMA) and lysergic acid diethylamide (LSD) may lead to potentially serious reactions if combined with Dapoxetine. These reactions include, but are not limited to arrhythmia, hyperthermia, and serotonin syndrome. Use of Dapoxetine with recreational drugs with sedative properties such as narcotics and benzodiazepines may further increase somnolence and dizziness.

Ethanol:
Combining alcohol with Dapoxetine may increase alcohol-related neurocognitive effects and may also enhance neurocardiogenic adverse events such as syncope, thereby increasing the risk of accidental injury; therefore, patients should be advised to avoid alcohol while taking Dapoxetine.

Syncope:
Possibly prodromal symptoms such as nausea, dizziness, lightheadedness, palpitations, asthenia, confusion and diaphoresis generally occurred within the first 3 hours following dosing and often preceded the syncope. Patients need to be made aware that they could experience syncope at any time with or without prodromal symptoms during their treatment with Dapoxetine.

Orthostatic hypotension:
An orthostatic test should be performed before initiating therapy. In case of a history of documented or suspected orthostatic reaction, treatment with Dapoxetine should be avoided.

Haemorrhage:
There have been reports of bleeding abnormalities with SSRIs. Caution is advised in patients taking Dapoxetine, particularly in concomitant use with medicinal products known to affect platelet function (e.g., atypical antipsychotics and phenothiazines, acetylsalicylic acid, nonsteroidal anti-inflammatory drugs [NSAIDs], anti-platelet agents) or anticoagulants (e.g., warfarin), as well as in patients with a history of bleeding or coagulation disorders.

PDE5 inhibitors:
The pharmacokinetics of Dapoxetine (60 mg) in combination with Tadalafil (20 mg) and Sildenafil (100 mg) were evaluated in a single dose crossover study. Tadalafil and Sildenafil did not affect the pharmacokinetics of Dapoxetine.

Tamsulosin:
Dapoxetine should be prescribed with caution in patients who use alpha adrenergic receptor antagonists due to possible reduced orthostatic tolerance.

Adverse effects:
The most common effects when taking dapoxetine are nausea, dizziness, dry mouth, headache, diarrhea, and insomnia. Discontinuation due to adverse effects is dose related. The rate of discontinuation is 0.3%, 1.7%, and 5.3% of 1067 studied subjects with placebo, Dapoxetine 30 mg, and Dapoxetine 60 mg respectively. Unlike others SSRIs used to treat depression, which have been associated with high incidences of sexual dysfunction, Dapoxetine is associated with low rates of sexual dysfunction. Taken as needed, Dapoxetine has very mild adverse effects on loss of libido (<1%) and ED (<4%).

Overdose:
No case of overdose has been reported. There were no unexpected adverse events in a clinical pharmacology study of Dapoxetine with daily doses up to 240 mg (two 120 mg doses given 3 hours apart). In general, symptoms of overdose with SSRIs include serotonin-mediated adverse reactions such as somnolence, gastrointestinal disturbances (such as nausea and vomiting), tachycardia, tremor, agitation and dizziness.

Withdrawal effects: Clinical trial in subjects with PE designed to assess the withdrawal effects of 62 days of daily or as needed dosing with 60 mg Dapoxetine showed no evidence of withdrawal syndrome.

Contraindications:
Hypersensitivity to the active substance or to any of the excipients.
Significant pathological cardiac conditions such as:
1. Heart failure (NYHA class II-IV)
2. Conduction abnormalities (second or third degree AV block or sick sinus syndrome) not treated with a permanent pace maker
3. Significant ischemic heart disease
4. Significant valvular disease.
5. Concomitant treatment with Monoamine Oxidase Inhibitors (MAOIs), or within 14 days of discontinuing treatment with a MAOI. Similarly, a MAOI should not be administered within 7 days after Dapoxetine has been discontinued.
6. Concomitant treatment with thioridazine, or within 14 days of discontinuing treatment with thioridazine. Similarly, thioridazine should not be administered within 7 days after Dapoxetine has been discontinued.
7. Concomitant treatment with serotonin reuptake inhibitors [selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs)] or other medicinal/herbal products with serotonergic effects [e.g., L-tryptophan, triptans, tramadol, linezolid, lithium, St John's Wort (Hypericum perforatum)] or within 14 days of discontinuing treatment with these medicinal/herbal products. Similarly, these medicinal/herbal products should not be administered within 7 days after Dapoxetine has been discontinued. Concomitant treatment of potent CYP3A4 inhibitors such as ketoconazole, itraconazole, ritonavir, saquinavir, telithromycin, nefazadone, nelfinavir, atazanavir etc.

Storage: Do not store above 30°C. Protect from light. Keep out of reach of children.

Packaging : PROLONG 30 : Each box contains 8's tablets in a blister strip.
PROLONG 60 : Each box contains 4's tablets in a blister strip.

Manufactured by

ZISKA PHARMA

Ziska Pharmaceuticals Ltd.
Kaliakoir, Gazipur, Bangladesh