

Dapoxetine Tablets 30 mg / 60 mg

DAPOX-GH® 30 / 60

Composition:

DAPOX-GH 30
Each film coated tablet contains:
Dapoxetine Hydrochloride
equivalent to Dapoxetine 30 mg
Colour: Approved colour used

DAPOX-GH 60

Each film coated tablet contains:
Dapoxetine Hydrochloride
equivalent to Dapoxetine 60 mg
Colour: Approved colour used

Pharmaceutical form

Film-coated tablet.

Therapeutic indications

Dapox-GH is indicated for the treatment of premature ejaculation (PE) in adult men aged 18 to 64 years.

- Dapox-GH should only be prescribed to patients who meet all the following criteria:
- An intravaginal ejaculatory latency time (IELT) of less than two minutes;
- Persistent or recurrent ejaculation with minimal sexual stimulation before, on, or shortly after penetration and before the patient wishes;
- Marked personal distress or interpersonal difficulty as a consequence of PE;
- Poor control over ejaculation; and
- A history of premature ejaculation in the majority of intercourse attempts over the prior 6 months.

Dapox-GH should be administered only as on-demand treatment before anticipated sexual activity. Dapox-GH should not be prescribed to delay ejaculation in men who have not been diagnosed with PE.

Posology and method of administration

Posology

Adult men (aged 18 to 64 years)

The recommended starting dose for all patients is 30 mg, taken as needed approximately 1 to 3 hours prior to sexual activity. Treatment with Dapox-GH should not be initiated with the 60 mg dose.

Dapox-GH is not intended for continuous daily use. Dapox-GH should be taken only when sexual activity is anticipated.

Dapox-GH must not be taken more frequently than once every 24 hours.

If the individual response to 30 mg is insufficient and the patient has not experienced moderate or severe adverse reactions or prodromal symptoms suggestive of syncope, the dose may be increased to a maximum recommended dose of 60 mg taken as needed approximately 1 to 3 hours prior to sexual activity. The incidence and severity of adverse events is higher with the 60 mg dose.

Method of administration

For oral use. Tablets should be swallowed whole to avoid the bitter taste.

Contraindications

- Hypersensitivity to the active substance Dapoxetine HCl

Significant pathological cardiac conditions such as:

- Heart failure (New York Heart Association class II-IV)
- Conduction abnormalities such as AV block or sick sinus syndrome
- Significant ischemic heart disease
- Significant valvular disease
- A history of syncope

Special warnings and precautions for use

Talk to your doctor, pharmacist or nurse before taking Dapox-GH if:

- You have not been diagnosed with premature ejaculation
- You also have another sexual problem, such as erectile dysfunction
- You have a history of dizziness from low blood pressure
- You use recreational drugs such as ecstasy, LSD, narcotics or benzodiazepines
- You drink alcohol

You have ever had a mental health problem such as depression, mania (symptoms include feeling overexcited, irritable or not being able to think clearly), bipolar disorder (symptoms include serious mood swings between mania and depression) or schizophrenia (a psychiatric disease)

You have epilepsy

You have a history of bleeding or blood clotting problems

You have kidney problems

You have high pressure in the eye (glaucoma). If any of the above apply to you (or you are not sure), talk to your doctor or pharmacist before taking this medicine.

Before you start taking this medicine, your doctor should perform a test to make sure that your blood pressure doesn't drop too much when you stand up from lying down.

Interaction with other medicinal products and other forms of interaction

Do not take Dapox-GH at the same time as any of the following medicines:

- Medicines for depression called 'monoamine oxidase inhibitors' (MAOIs)

Thioridazine used for schizophrenia

Other medicines for depression

Lithium a medicine for bipolar disorder

Linezolid an antibiotic used to treat infections

Tryptophan a medicine to help you sleep

St. John's wort a herbal medicine

Tramadol used to treat serious pain

Medicines used to treat migraines. Do not take Dapox-GH at the same time as any of the medicines listed above. If you have taken any of these medicines, you will need to wait 14 days after you stop taking it before you can start taking Dapox-GH. Once you have stopped taking Dapox-GH, you will need to wait 7 days before taking any of the medicines listed above. If you are not sure about what to do, talk to your doctor or pharmacist before taking this medicine.

Certain medicines for fungal infection, including ketoconazole and itraconazole

Certain medicines for HIV, including ritonavir, saquinavir, nevirapine and atazanavir

Certain antibiotics for treating infection, including telithromycin

Nefazodone an antidepressant.

Tell your doctor or pharmacist if you are taking any of the following medicines:

Medicines for mental health problems other than depression

Nonsteroidal anti-inflammatory medicines such as ibuprofen or acetylsalicylic acid

Medicines to thin your blood, such as warfarin

Certain medicines used to treat erectile dysfunction, such as sildenafil, tadalafil or vardenafil, as these medicines may lower your blood pressure, possibly upon standing

Certain medicines used to treat high blood pressure and chest pain (angina) (such as verapamil and diltiazem), or enlarged prostate, as these medicines may also lower your blood pressure, possibly upon standing

Certain other medicines for fungal infection, such as fluconazole

Certain other medicines for HIV, such as ampravir and fosamprenavir

Certain other antibiotics for treating infection, such as erythromycin and clarithromycin

Aprepitant used to treat nausea. If you are not sure if any of the above apply to you, talk to your doctor or pharmacist before taking this medicine. Dapox-GH with food, drink and alcohol

Do not drink grapefruit juice within 24 hours prior to taking this medicine as this can increase the level of this medicine in your body.

This medicine can be taken with or without food.

You should take this medicine with at least one full glass of water.

Avoid alcohol when taking this medicine.

The effects of alcohol such as feeling dizzy, sleepy and having slow reactions, may be increased if taken with this medicine.

Drinking alcohol while taking this medicine may increase your risk of injury from fainting or from other side effects.

Fertility, pregnancy and lactation

Dapox-GH is not indicated for use by women.

Animal studies do not indicate direct or indirect harmful effects with respect to fertility, pregnancy or embryonal/foetal development.

It is not known if either dapoxetine or its metabolites are excreted in human milk.

Effects on ability to drive and use machines

Dapox-GH has minor or moderate influence on the ability to drive and use machines. Dizziness, disturbance in attention, syncope, blurred vision and somnolence have been reported in subjects receiving dapoxetine in clinical

trials. Therefore, patients should be warned to avoid situations where injury could result, including driving or operating hazardous machinery.

4.8 Undesirable effects

Table 1: Frequency of Adverse Reactions (MedDRA)

System Organ Class	Very common (> 1/10)	Common (≥ 1/100 to < 1/10)	Uncommon (≥ 1/1000 to < 1/100)	Rare (≥ 1/10000 to < 1/1000)
Psychiatric disorders	Anxiety, Agitation, Restlessness, Insomnia, Abnormal dreams, Libido decreased	Depression, Depressed mood, Euphoric mood, Mood altered, Nervousness, Indifference, Apathy, Confusional state, Disorientation, Thinking abnormal, Hypervigilance, Sleep disorder, Initial insomnia, Middle insomnia, Nightmare, Bruxism, Loss of libido, Anorgasmia	-	-
Nervous system disorders	Dizziness, Headache, Somnolence, Disturbance in attention, Tremor, Paraesthesia	Syncope, Syncope vasovagal, Dizziness postural, Akathisia, Dysgeusia, Hypersomnia, Lethargy, Sedation, Depressed level of consciousness	Dizziness exertional, Sudden onset of sleep	-
Eye disorders	Vision blurred	Mydriasis, Eye pain, Visual disturbance	-	-
Ear and labyrinth disorders	Tinnitus	Vertigo	-	-
Cardiac disorders		Sinus arrest, Sinus bradycardia, Tachycardia	-	-
Vascular disorders	Flushing	Hypotension, Systolic hypertension, Hot flush	-	-
Respiratory, thoracic and mediastinal disorders	Sinus congestion, Yawning	-	-	-
Gastrointestinal disorders	Nausea	Diarrhoea, Vomiting, Constipation, Abdominal pain, Upper, Dyspepsia, Flatulence, Stomach discomfort, Abdominal distension, Dry mouth	Abdominal discomfort, Epigastric discomfort	Defaecation urgency
Skin and subcutaneous tissue disorders		Pruritis, Cold sweat	-	-
Reproductive system and breast disorders		Ejaculation failure, Male orgasmic disorder, Paresthesia of genital male	-	-
General disorders and administration site conditions	Fatigue, Irritability	Asthenia, Feeling hot, Feeling jittery, Feeling abnormal, Feeling drunk	-	-
Investigations	Blood pressure increased	Heart rate increased, Blood pressure diastolic increased, Blood pressure orthostatic increased	-	-

Overdose

No case of overdose has been reported.

There were no unexpected adverse events in a clinical pharmacology study of Dapox-GH 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.

In cases of overdose, standard supportive measures should be adopted as required. Due to high protein binding and large volume of distribution of dapoxetine hydrochloride, forced diuresis, dialysis, hemoperfusion and exchange transfusion are unlikely to be of benefit. No specific antidotes for Dapox-GH are known.

Pharmacodynamic properties

Pharmaco-therapeutic group: Other Urologicals, ATC code: G04BX14

Mechanism of action

Dapoxetine is a potent selective serotonin reuptake inhibitor (SSRI) with an IC₅₀ of 1.12 nM, while its major human metabolites, desmethyl-dapoxetine (IC₅₀ < 1.0 nM) and di-desmethyl-dapoxetine (IC₅₀ = 2.0 nM) are equivalent or less potent (dapoxetine-N-oxide (IC₅₀ = 262 nM)).

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).

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 postsynaptic receptors.

Pharmacokinetic properties

Absorption

Dapoxetine hydrochloride is rapidly absorbed with maximum plasma concentrations (C_{max}) occurring approximately 1-2 hours after tablet intake. The absolute bioavailability is 42% (range 15-76%), and dose proportional increases in exposure (AUC and C_{max}) are observed between the 30 and 60 mg dose strengths. Following multiple doses, AUC values for both dapoxetine and the active metabolite desmethyl-dapoxetine (DED) increase by approximately 50% when compared to single dose AUC values.

Ingestion of a high fat meal modestly reduced the C_{max} (by 10%) and modestly increased the AUC (by 12%) of dapoxetine and slightly delayed the time for dapoxetine to reach peak concentrations. These changes are not clinically significant. Dapox-GH can be taken with or without food.

Distribution

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 has a mean steady state volume of distribution of 162 L.

Biotransformation

In vitro studies suggest that dapoxetine is cleared by multiple enzyme systems in the liver and kidneys, primarily CYP2D6, CYP3A4, and flavin monooxygenase (FMQ1). Following oral dosing of ¹⁴C-dapoxetine, dapoxetine was extensively metabolized to multiple metabolites primarily through the following biotransformation pathways: N-oxidation, N-demethylation, naphthyl hydroxylation, glucuronidation and sulfation. There was evidence of presystemic first-pass metabolism after oral administration.

Elimination

The metabolites of dapoxetine were primarily eliminated in the urine as conjugates. Unchanged active substance was not detected in the urine. Following oral administration, dapoxetine has an initial (disposition) half-life of approximately 1.5 hours, with plasma levels less than 5% of peak concentrations by 24 hours post-dose, and a terminal half-life of approximately 19 hours. The terminal half-life of DED is approximately 19 hours.

Storage Instructions

Store below 30°C. Protect from moisture.

Keep out of reach of children.

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® Trade mark.

160383

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DAPOX-GH 30 / 60

Composition:

DAPOX-GH 30

Chaque comprimé pelliculé contient:
Chlorhydrate de dapoxétine
équivalent à Dapoxetine 30 mg

Couleur: couleur approuvée utilisée

DAPOX-GH 60

Chaque comprimé pelliculé contient:
Chlorhydrate de dapoxétine
équivalent à Dapoxetine 60 mg

Couleur: couleur approuvée utilisée

Forme pharmaceutique

Comprimé pelliculé.</p