

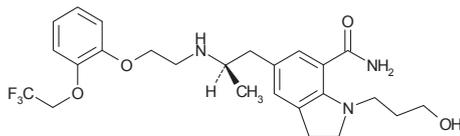
Silorap™

[Silodosin]

سیلوریپ

Capsules 8mg

Silorap (Silodosin) is a selective antagonist of alpha-1 adrenoreceptors. The chemical name of silodosin is 1-(3-Hydroxypropyl)-5-[(2R)-2-[(2-{2-(2,2,2-trifluoroethoxy) phenoxy}ethyl)amino] propyl]-2,3-dihydro-1H-indole-7-carboxamide. Its molecular formula is $C_{28}H_{32}F_3N_3O_4$ and the structural formula is:



Silodosin

QUALITATIVE AND QUANTITATIVE COMPOSITION

Silorap (Silodosin) is available for oral administration as:

Silorap Capsules 8mg
Each capsule contains:
Silodosin...8mg

CLINICAL PHARMACOLOGY

Mechanism of Action

Silodosin is a selective antagonist of post-synaptic alpha-1 adrenoreceptors, which are located in the human prostate, bladder base, bladder neck, prostatic capsule and prostatic urethra. Blockade of these alpha-1 adrenoreceptors can cause smooth muscle in these tissues to relax, resulting in an improvement in urine flow and a reduction in benign prostatic hyperplasia (BPH) symptoms.

Pharmacokinetic

Absorption

Silodosin administered orally is well absorbed and absorption is dose proportional. The absolute bioavailability is approximately 32%. Food decreases C_{max} by approximately 30%, increases t_{max} by approximately 1 hour and has little effect on AUC.

Distribution

Silodosin has an apparent volume of distribution of 49.5L and is approximately 97% protein bound.

Metabolism

Silodosin undergoes extensive metabolism through glucuronidation, alcohol and aldehyde dehydrogenase and cytochrome P450 3A4 (CYP3A4) pathways. The main metabolite of silodosin is a glucuronide conjugate (KMD-3213G) that is formed via direct conjugation of silodosin by UDP-glucuronosyltransferase 2B7 (UGT2B7). KMD-3213G, which has been shown in vitro to be active, has an extended half-life (approximately 24 hours) and reaches plasma exposure (AUC) approximately 4 times greater than that of silodosin. The second major metabolite (KMD-3293) is formed via alcohol and aldehyde dehydrogenases and reaches plasma exposures similar to that of silodosin. KMD-3293 is not expected to contribute significantly to the overall pharmacologic activity of silodosin.

Excretion

Following oral administration of ¹⁴C-labeled silodosin, the recovery of radioactivity after 10 days was approximately 33.5% in urine and 54.9% in feces. After intravenous administration, the plasma clearance of silodosin was approximately 10 L/hour.

Special Population

Geriatric Patients

The exposure (AUC) and elimination half-life of silodosin were approximately 10% less and 17% greater, respectively, in geriatric males 65 to 75 years of age than the younger subjects and approximately 16% less and 35% greater, respectively in geriatric males > 75 years of age than the younger subjects. A decrease in C_{max} of 13% and 40% was seen in males 65 to 75 years of age and > 75 years of age, respectively.

Renal impairment

Exposure to silodosin (unbound) in subjects with mild and moderate renal impairment resulted, on average, in an increase of C_{max} (1.6-fold) and AUC (1.7-fold) relative to subjects with normal renal function. In subjects with severe renal impairment increase of exposure was 2.2-fold for C_{max} and 3.7-fold for AUC. Exposure to the main metabolites, silodosin glucuronide and KMD3293, was also increased.

Pediatric

Safety and effectiveness of silodosin on pediatric patients have not been established.

THERAPEUTIC INDICATIONS

Silorap (Silodosin) is indicated for the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH).

DOSAGE & ADMINISTRATION

Recommended Dose

Silorap (Silodosin) 8mg once daily with a meal is recommended as the dose for the treatment of the signs and symptoms of BPH.

Missed Dose

If a dose of Silorap (Silodosin) is missed, the missed dose can be taken later the same day. If a day is missed, the missed dose should be skipped and the regular dosing schedule should be resumed. Doses must not be doubled.

Administration

Silorap (Silodosin) should be taken orally once daily with a meal. Silorap (Silodosin) capsules may also be administered by carefully opening the capsule and sprinkling the powder inside on a spoonful of applesauce. The applesauce should be swallowed immediately without chewing and followed with a glass of cool water to ensure complete swallowing of the powder. The applesauce used should not be hot and it should be soft enough to be swallowed without chewing. Any powder/applesauce mixture should be used immediately and not stored for future use.

Special Population

Renal impairment

In patients with moderate renal impairment, the dose should be reduced to 4mg once daily taken with a meal. No dosage adjustment is needed in patients with mild renal impairment.

Hepatic impairment

No dosage adjustment is needed in patients with mild or moderate hepatic impairment.

Geriatric

No dosage adjustment is needed in elderly patients.

ADVERSE REACTIONS

Very Common

Ejaculatory disorders, including retrograde ejaculation and anejaculation.

Common

Dizziness, orthostatic hypotension, nasal congestion and diarrhoea.

Uncommon

Libido decreased, tachycardia, hypotension, nausea, dry mouth, abnormal liver function tests, skin rash, pruritus, urticaria, drug eruption, erectile dysfunction and Intraoperative Floppy Iris Syndrome.

Rare

Syncope, loss of consciousness and palpitations.

Very Rare

Allergic type reactions including facial swelling, swollen tongue and pharyngeal oedema.

"To report SUSPECTED ADVERSE REACTIONS to Getz Pharma's Pharmacovigilance Section, please contact at dsafety@getzpharma.com or +92-21-38636363"

CONTRAINDICATIONS

Silodosin is contraindicated:

- In patients with known hypersensitivity to silodosin or to any excipient of the product.
- In patients with severe renal impairment.
- In patients with severe hepatic impairment.
- Concomitant administration with strong Cytochrome P450 3A4 (CYP3A4) inhibitors (e.g., ketoconazole, clarithromycin, itraconazole, ritonavir).
- Silodosin should not be administered to patients using concomitant alpha-blockers (e.g., prazosin, terazosin, doxazosin).

PRECAUTIONS

- As with all alpha-1 antagonists, a reduction in blood pressure can occur in individual cases during treatment with silodosin, as a result of which, rarely, syncope can occur. At the first signs of orthostatic hypotension (dizziness, weakness), the patient should sit or lie down until the symptoms have disappeared.
- Carcinoma of the prostate and BPH cause many of the same symptoms. These two diseases frequently co-exist. Therefore, patients thought to have BPH should be examined prior to starting therapy with silodosin to rule out the presence of carcinoma of the prostate.
- Intraoperative Floppy Iris Syndrome has been observed during cataract surgery in some patients on alpha-1 blockers or previously treated with alpha-1 blockers. Patients planning cataract surgery should be told to inform their ophthalmologist that they are taking silodosin.
- Treatment with silodosin leads to a decrease in the amount of semen released during orgasm that may temporarily affect male fertility. This effect disappears after discontinuation of silodosin.
- Silodosin has minor or moderate influence on the ability to drive and use machines. Patients should be informed about the possible occurrence of symptoms related to postural hypotension (such as dizziness) and should be cautioned about driving or operating machines until they know how silodosin will affect them.
- Exercise caution and monitor patients with moderate renal impairment for adverse events.

Pregnancy & Nursing Mothers

Silodosin is not indicated nor recommended for use in women.

DRUG INTERACTIONS

Moderate CYP3A4 Inhibitors

Concomitant administration with moderate CYP3A4 inhibitors (e.g., diltiazem, erythromycin, verapamil) may increase concentration of silodosin. Exercise caution and monitor patients for adverse events when co-administering silodosin with moderate CYP3A4 inhibitors.

Strong P-glycoprotein (P-gp) Inhibitors

Inhibition of P-gp may lead to increased silodosin concentration. Silodosin is therefore not recommended in patients taking strong P-gp inhibitors such as cyclosporine.

Antihypertensives

Exercise caution during concomitant use with antihypertensives and monitor patients for possible adverse events.

PDE-5 Inhibitors

Patients taking PDE-5 Inhibitors concomitantly with silodosin should be monitored for possible adverse events. Silodosin can potentially cause symptomatic hypotension.

OVERDOSAGE

Adverse event reported with silodosin overdose was postural hypotension.

Treatment

Should overdose of silodosin lead to hypotension, support of the cardiovascular system is of first importance. Restoration of blood pressure and normalization of heart rate may be accomplished by maintaining the patient in the supine position. If this measure is inadequate, administration of intravenous fluid should be considered. If necessary, vasopressors could be used and renal function should be monitored and supported as needed. Dialysis is unlikely to be of significant benefit since silodosin is highly (97%) protein bound.

STORAGE

Do not store above 30°C.
Protect from light and moisture.
The expiration date refers to the product correctly stored at the required conditions.

HOW SUPPLIED

Silorap (Silodosin) Capsules 8mg are available in blister pack of 10's.

Keep out of reach of children.

To be sold on prescription of a registered medical practitioner only.

Please read the contents carefully before use.
This package insert is continually updated from time to time.

Manufactured by:



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pharma
(PVT) LIMITED | 29-30/27,
www.getzpharma.com | K.I.A., Karachi,
Pakistan

L-200010557