SILODOSIN

℞

URELEVE®
2mg Capsule
4mg Capsule
8mg Capsule
ALPHA 1-ADRENORECEPTOR ANTAGONIST

FORMULATION
Each capsule contains:
Silodosin …… 2mg
Silodosin …… 4mg
Silodosin …… 8mg

DESCRIPTION
2mg – Ivory/Ivory, hard gelatin capsules of size "3" self-locking, containing white coloured, granular powder.
4mg – Orange/White, hard gelatin capsules of size "3" self-locking, containing white coloured, granular powder.
8mg – Pink/White, hard gelatin capsules of size "3" self-locking, containing white coloured, granular powder.

PHARMACOLOGICAL PROPERTIES

Mechanism of Action
Silodosin is a selective antagonist of post-synaptic alpha-1 adrenoceptors, which are located in the human prostate, bladder base, bladder neck, prostatic capsule, and prostatic urethra. Blockade of these alpha-1 adrenoceptors can cause smooth muscle in theses tissue to relax, resulting in an improvement in urine flow and a reduction in BPH symptoms.
An *in vitro* study examining binding affinity of silodosin to the three subtypes of the alpha-1 adrenoceptors (alpha-1A, alpha-1B, and alpha-1D) was conducted. The results of the study demonstrated that Silodosin binds with high affinity to the alpha-1A subtype.

PHARMACODYNAMICS
Orthostatic Effects
A test for postural hypotension was conducted 2 to 6 hours after the first dose in the two 12-week, double-blind, placebo-controlled clinical studies. After the patient had been at rest in a supine position for 5 minutes, the patient was asked to stand. Blood pressure and heart rate were assessed at 1 minute and 3 minutes after standing. A positive result was defined as a > 30 mmHg decrease in systolic blood pressure, or a > 20 mmHg decrease in diastolic blood pressure, or a > 20 bpm increase in heart rate.

Table 2 Summary of Orthostatic Test Results in 12-week, Placebo-Controlled Clinical Trials

Time of Measurement	Test Result	SILODOSIN N=466 n (%)	Placebo N=457 n (%)
1 Minute After Standing	Negative	459 (98.7)	454 (99.6)
	Positive	6 (1.3)	2 (0.4)
3 Minutes After Standing	Negative	456 (98.1)	454 (99.6)
	Positive	9 (1.9)	2 (0.4)

Cardiac Electrophysiology
The effect of Silodosin on QT interval was evaluated in a double-blind, randomized, active-(moxifloxacin) and placebo-controlled, parallel-group study in 189 healthy male subjects aged 18 to 45 years. Subjects received either Silodosin 8 mg, Silodosin 24 mg, or placebo once daily for five days, or a single dose of moxifloxacin 400 mg on Day 5 only. The 24 mg dose of Silodosin was selected to achieve blood levels of Silodosin that may be seen in "worst-case" scenario exposure (i.e., in the setting of concomitant renal disease or use of strong CYP3A4 inhibitors) (mentioned in sections 4.3, 4.4, 4.5 & 5.1 of SmPC). QT interval was measured during a 24-hour period following dosing on Day 5 (at Silodosin steady state).
Silodosin was not associated with an increase in individual corrected (QTcI) QT interval at any time during steady state measurement, while moxifloxacin, the active control, was associated with a maximum 9.59 msec increase in QTcI.

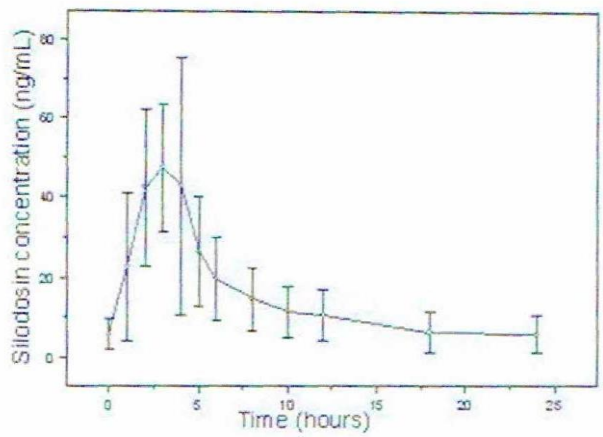
Pharmacokinetics
The pharmacokinetics of Silodosin have been evaluated in adult male subjects with doses ranging from 0.1 mg to 24 mg per day. The pharmacokinetics of Silodosin are linear throughout this dosage range.
Absorption
The pharmacokinetic characteristics of Silodosin 8 mg once daily were determined in a multi-dose, open-label, 7-day pharmacokinetic study completed in 19 healthy, target-aged (≥ 45 years of age) male subjects. Table 3 presents the steady state pharmacokinetics of this study.

Table 3 Mean (±SD) Steady State Pharmacokinetic Parameters in Healthy Males Following Silodosin 8 mg Once Daily with Food

C_{max} (ng/mL)	T_{max} (hours)	$t_{1/2}$ (hours)	AUC_{ss} (ng•hr/mL)
61.6 ± 27.54	2.6 ± 0.90	13.3 ± 8.07	373.4 ± 164.94

C_{max} = maximum concentration, t_{max} = time to reach C_{max}, $t_{1/2}$ = elimination half-life,
AUC_{ss} = steady state area under the concentration-time curve

Figure 1 Mean (±SD) Silodosin Steady State Plasma Concentration-Time Profile in Healthy Target-Aged Subjects Following Silodosin 8 mg Once Daily with Food



The absolute bioavailability is approximately 32%.

Food Effect

The maximum effect of food (i.e., co-administration with a high fat, high calorie meal) on the PK of Silodosin was not evaluated. The effect of a moderate fat, moderate calorie meal was variable and decreased Silodosin C_{max} by approximately 18 to 43% and AUC by 4 to 49% across three different studies.

In a single-center, open-label, single-dose, randomized, two-period crossover study in twenty healthy male subjects age 21 to 43 years under fed conditions, a study was conducted to evaluate the relative bioavailability of the contents of an 8 mg capsule (size #1) of Silodosin sprinkled on applesauce compared to the product administered as an intact capsule. Based on AUC_{0-24} and C_{max}, Silodosin administered by sprinkling the contents of a Silodosin capsule onto a tablespoonful of applesauce was found to be bioequivalent to administering the capsule whole.

Distribution

Silodosin has an apparent volume of distribution of 49.5 L 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). Co-administration with inhibitors of UGT2B7 (e.g., probenecid, valproic acid, fluconazole) may potentially increase exposure to Silodosin. 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 four 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 ^{14}C-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 Populations

Race

No clinical studies specifically investigating the effects of race have been performed.

Geriatric

In a study comparing 12 geriatric males (mean age 69 years) and 9 young males (mean age 24 years), the exposure (AUC) and elimination half-life of Silodosin were approximately 15% and 20%, respectively, greater in geriatric than young subjects. No difference in the C_{max} of Silodosin was observed.

Pediatric

Silodosin has not been evaluated in patients less than 18 years of age.

Renal Impairment

In a study with six subjects with moderate renal impairment, the total Silodosin (bound and unbound) AUC, C_{max}, and elimination half-life were 3.2-, 3.1-, and 2-fold higher, respectively, compared to seven subjects with normal renal function. The unbound Silodosin AUC and C_{max} were 2.0- and 1.5-fold higher, respectively, in subjects with moderate renal impairment compared to the normal controls.

In controlled and uncontrolled clinical studies, the incidence of orthostatic hypotension and dizziness was greater in subjects with moderate renal impairment treated with 8 mg Silodosin daily than in subjects with normal or mildly impaired renal function.

Hepatic Impairment

In a study comparing nine male patients with moderate hepatic impairment (Child-Pugh scores 7 to 9), to nine healthy male subjects, the single dose pharmacokinetic disposition of Silodosin was not significantly altered in patients with moderate hepatic impairment. No dosing adjustment is required in patients with mild or moderate hepatic impairment. The pharmacokinetics of Silodosin in patients with severe hepatic impairment have not been studied.

Drug Interactions

Cytochrome P450 (CYP) 3A4 Inhibitors

Two clinical drug interaction studies were conducted in which a single oral dose of Silodosin was co-administered with strong CYP3A4 inhibitor, ketoconazole, at doses of 400 mg and 200 mg, respectively, once daily for 4 days. Co-administration of 8 mg Silodosin with 400 mg ketoconazole led to 3.8-fold increase in Silodosin C_{max} and 3.2-fold increase in AUC. Co-administration of 4 mg Silodosin with 200 mg ketoconazole led to similar increases: 3.7- and 2.9-fold in Silodosin C_{max} and AUC, respectively. Silodosin is contraindicated with strong CYP3A4 inhibitors.

The effect of moderate CYP3A4 inhibitors on the pharmacokinetics of Silodosin has not been evaluated. Due to the potential for increased exposure to Silodosin, caution should be exercised when co-administering Silodosin with moderate CYP3A4 inhibitors, particularly those that also inhibit P-glycoprotein (e.g., verapamil, erythromycin).

P-glycoprotein (P-gp) inhibitors
In-vitro studies indicated that Silodosin is a P-gp substrate. A drug interaction study with strong P-gp inhibitor has not been conducted. However, in drug interaction studies with ketoconazole, a CYP3A4 inhibitor that also inhibits P-gp, significant increase in exposure to Silodosin was observed. Inhibition of P-gp may lead to increased Silodosin concentration. Silodosin is not recommended in patients taking strong P-gp inhibitors (e.g., cyclosporine).
Digoxin
The effect of Silodosin on the pharmacokinetics of digoxin was evaluated in a multiple dose, single-sequence, crossover study of 16 healthy males, aged 18 to 45 years. A loading dose of digoxin was administered as 0.5 mg twice daily for one day. Following the loading doses, digoxin (0.25 mg once daily) was administered alone for seven days and then concomitantly with Silodosin 4 mg twice a day for the next seven days. No significant differences in digoxin AUC and C_{max} were observed when digoxin was administered alone or concomitantly with Silodosin.
Other Metabolic Enzymes and Transporters
In vitro studies indicated that Silodosin administration is not likely to inhibit the activity of CYP1A2, CYP2A6, CYP2C9, CYP2C19, CYP2D6, CYP2E1, and CYP3A4 or induce the activity of CYP1A2, CYP2C8, CYP2C9, CYP2C19, CYP3A4, and P-gp.

Preclinical Safety data

In a 2-year oral carcinogenicity study in rats administered doses up to 150 mg/kg/day [about 8 times the exposure of the maximum recommended human dose (MRHE) based on AUC of Silodosin], an increase in thyroid follicular cell tumor incidence was seen in male rats receiving doses of 150 mg/kg/day. Silodosin induced stimulation of thyroid stimulating hormone (TSH) secretion in the male rat as a result of increased metabolism and decreased circulating levels of thyroxine (T4). These changes are believed to produce specific morphological and functional changes in the rat thyroid including hypertrophy, hyperplasia, and neoplasia. Silodosin did not alter TSH or T4 levels in clinical trials and no effects based on thyroid examinations were noted. The relevance to human risk of these thyroid tumors in rats is not known.
In a 2-year oral carcinogenicity study in mice administered doses up to 100 mg/kg/day in males (about nine times the MRHE based on AUC of Silodosin) and 400 mg/kg/day in females (about 72 times the MRHE based on AUC), there were no significant tumor findings in male mice. Female mice treated for 2 years with doses of 150 mg/kg/day (about 29 times the MRHE based on AUC) or greater had statistically significant increases in the incidence of mammary gland adenoacanthomas and adenocarcinomas. The increased incidence of mammary gland neoplasms in female mice was considered secondary to Silodosin-induced hyperprolactinemia measured in the treated mice. Elevated prolactin levels were not observed in clinical trials. The relevance to human risk of prolactin-mediated endocrine tumors in mice is not known. Rats and mice do not produce glucuronidated Silodosin, which is present in human serum at approximately four times the level of circulating Silodosin and which has similar pharmacological activity to Silodosin.

INDICATION

Silodosin is a selective alpha-1 adrenergic receptor antagonist, indicated for the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH). Silodosin is not indicated for the treatment of hypertension.

CONTRAINDICATIONS

Silodosin is contraindicated with the following patient's condition:

- Severe renal impairment (CCr < 30 mL/min) (mentioned in section 4.3 and 4.4 of SmPC).
- Severe hepatic impairment (Child-Pugh score ≥ 10)
- Concomitant administration with strong Cytochrome P450 3A4 (CYP3A4) inhibitors (e.g., ketoconazole, clarithromycin, itraconazole, ritonavir) (mentioned in sections 4.3, 4.4, 4.5 & 5.1 of SmPC).
- Patients with a history of hypersensitivity to Silodosin or any of the ingredients of Silodosin

DOSAGE AND ADMINISTRATION

The recommended dose is 8 mg orally once daily with a meal. Or as prescribed by the physician.
Patients who have difficulty swallowing pills and capsules may carefully open the Silodosin capsule and sprinkle the powder inside on a tablespoon of applesauce. The applesauce should be swallowed immediately (within 5 minutes) without chewing and followed with an 8 oz 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 (within 5 minutes) and not stored for future use. Subdividing the contents of a Silodosin capsule is not recommended.
Dosage Adjustment in Special Populations
Renal impairment: Silodosin is contraindicated in patients with severe renal impairment (CCr <30 mL/min). In patients with moderate renal impairment (CCr 30-50 mL/min), the dose should be reduced to 4 mg once daily taken with a meal. No dosage adjustment is needed in patients with mild renal impairment (CCr 50-80 mL/min).
Hepatic impairment: Silodosin has not been studied in patients with severe hepatic impairment (Child-Pugh score ≥ 10) and is therefore contraindicated in these patients. No dosage adjustment is needed in patients with mild or moderate hepatic impairment.

WARNINGS AND PRECAUTIONS

Orthostatic Effects
Postural hypotension, with or without symptoms (e.g., dizziness) may develop when beginning Silodosin treatment. As with other alpha-blockers, there is potential for syncope. Patients should be cautioned about driving, operating machinery, or performing hazardous tasks when initiating therapy (mentioned in sections 4.4 & 4.8 of SmPC).
Renal Impairment
In a clinical pharmacology study, plasma concentrations (AUC and C_{max}) of Silodosin were approximately three times higher in subjects with moderate renal impairment compared with subjects with normal renal function, while half-lives of Silodosin doubled in duration. The dose of Silodosin should be reduced to 4 mg in patients with moderate renal impairment. Exercise caution and monitor such patients for adverse events. Silodosin is contraindicated in patients with severe renal impairment (mentioned in sections 4.3 & 4.4 of SmPC).
Hepatic Impairment
Silodosin has not been tested in patients with severe hepatic impairment, and therefore, should not be prescribed to such patients.
Pharmacokinetic Drug-Drug Interactions
In a drug interaction study, co-administration of a single 8 mg dose of Silodosin with 400 mg ketoconazole, a strong CYP3A4 inhibitor, caused a 3.8-fold increase in maximum plasma Silodosin concentrations and 3.2-fold increase in silodosin exposure (i.e., AUC). Concomitant use of ketoconazole or other strong CYP3A4 inhibitors (e.g., itraconazole, clarithromycin, ritonavir) is therefore contraindicated (mentioned in sections 4.3, 4.4, 4.5 & 5.1 of SmPC).
Pharmacodynamic Drug-Drug Interactions
The pharmacodynamic interactions between silodosin and other alpha-blockers have not been determined. However, interactions may be expected, and Silodosin should not be used in combination with other alpha-blockers (mentioned in sections 4.4 & 4.5 of SmPC).
A specific pharmacodynamic interaction study between silodosin and antihypertensive agents has not been performed. However, patients in the Phase 3 clinical studies taking concomitant antihypertensive medications with Silodosin did not experience a significant increase in the incidence of syncope, dizziness, or orthostasis (mentioned in sections 4.4 & 4.8 of SmPC). Nevertheless, exercise caution during concomitant use with antihypertensive and monitor patients for possible adverse events (mentioned in sections 4.4 & 4.5 of SmPC).
Caution is also advised when alpha-adrenergic blocking agents including Silodosin are co-administered with PDE5 inhibitors. Alpha-adrenergic blockers and PDE5 inhibitors are both vasodilators that can lower blood pressure. Concomitant use of these two drug classes can potentially cause symptomatic hypotension (mentioned in sections 4.4 & 4.5 of SmPC).
Carcinoma of the Prostate
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 (mentioned in section 4.4 of SmPC).

Intraoperative Floppy Iris Syndrome

Intraoperative Floppy Iris Syndrome has been observed during cataract surgery in some patients on alpha-1 blockers or previously treated with alpha-1 blockers. This variant of small pupil syndrome is characterized by the combination of a flaccid iris that billows in response to intraoperative irrigation currents; progressive intraoperative miosis despite preoperative dilation with standard mydriatic drugs; and potential prolapse of the iris toward the phacoemulsification incisions. Patients planning cataract surgery should be told to inform their ophthalmologist that they are taking Silodosin (mentioned in sections 4.4 & 4.8 of SmPC).

Laboratory Test Interactions

No laboratory test interactions were observed during clinical evaluations. Treatment with Silodosin for up to 52 weeks had no significant effect on prostate-specific antigen (PSA).

PREGNANCY AND LACTATION

Pregnancy

Pregnancy Category B. Silodosin is not indicated for use in women.

An embryo/fetal study in rabbits showed decrease maternal body weight at 200 mg/kg/day (approximately 13 to 25 times the maximum recommended human exposure or MRHE of Silodosin via AUC). No statistically significant teratogenicity was observed at this dose.

Silodosin was not teratogenic when administered to pregnant rats during organogenesis at 1000 mg/kg/day (estimated to be approximately 20 times the MRHE). No maternal or fetal effects were observed at this dose. Rats and rabbits do not produce glucuronidated Silodosin, which is present in human serum at approximately 4 times the level of circulating Silodosin and which has similar pharmacological activity to Silodosin.

No effects on physical or behavioral development of offspring were observed when rats were treated during pregnancy and lactation at up to 300 mg/kg/day.

Pediatric Use

Silodosin is not indicated for use in pediatric patients. Safety and effectiveness in pediatric patients have not been established.

Geriatric Use

In double-blind, placebo-controlled, 12-week clinical studies of Silodosin, 259 (55.6%) were under 65 years of age, 207 (44.4%) patients were 65 years of age and over, while 60 (12.9%) patients were 75 years of age and over. Orthostatic hypotension was reported in 2.3% of Silodosin patients < 65 years of age (1.2% for placebo), 2.9% of Silodosin patients ≥ 65 years of age (1.9% for placebo), and 5.0% of patients ≥ 75 years of age (0% for placebo). There were otherwise no significant differences in safety or effectiveness between older and younger patients**.**

Renal Impairment

The effect of renal impairment on Silodosin pharmacokinetics was evaluated in a single dose study of six male patients with moderate renal impairment and seven male subjects with normal renal function. Plasma concentrations of Silodosin were approximately three times higher in subjects with moderate renal impairment compared with subjects with normal renal function.

Silodosin should be reduced to 4 mg per day in patients with moderate renal impairment. Exercise caution and monitor patients for adverse events.

Silodosin has not been studied in patients with severe renal impairment. Silodosin is contraindicated in patients with severe renal impairment.

Hepatic Impairment

In a study comparing nine male patients with moderate hepatic impairment (Child-Pugh scores 7 to 9), to nine healthy male subjects, the single dose pharmacokinetics of Silodosin were not significantly altered in patients with hepatic impairment. No dosing adjustment is required in patients with mild or moderate hepatic impairment.

Silodosin has not been studied in patients with severe hepatic impairment. Silodosin is contraindicated in patients with severe hepatic impairment.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINE

One of the adverse effects is dizziness; patients are advised to refrain from driving and operating machinery.

DRUG INTERACTIONS

Moderate and Strong CYP3A4 Inhibitors

In a clinical metabolic inhibition study, a 3.8-fold increase in silodosin maximum plasma concentrations and 3.2-fold increase in Silodosin exposure were observed with concurrent administration of a strong CYP3A4 inhibitor, 400 mg ketoconazole. Use of strong CYP3A4 inhibitors such as itraconazole or ritonavir may cause plasma concentrations of Silodosin to increase. Concomitant administration of strong CYP3A4 inhibitors and Silodosin is contraindicated.

The effect of moderate CYP3A4 inhibitors on the pharmacokinetics of silodosin has not been evaluated. 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 (mentioned in sections 4.3, 4.4, 4.5 & 5.1 of SmPC).

Strong P-glycoprotein (P-gp) Inhibitors

In vitro studies indicated that Silodosin is a P-gp substrate. Ketoconazole, a CYP3A4 inhibitor that also inhibits P-gp, caused significant increase in exposure to Silodosin. 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.

Alpha-Blockers

The pharmacodynamic interactions between Silodosin and other alpha-blockers have not been determined. However, interactions may be expected, and Silodosin should not be used in combination with other alpha-blockers (mentioned in sections 4.4 & 4.5 of SmPC).

Digoxin

The effect of co-administration of Silodosin and digoxin 0.25 mg/day for 7 days was evaluated in a clinical trial in 16 healthy males, aged 18 to 45 years. Concomitant administration of Silodosin and digoxin did not significantly alter the steady state pharmacokinetics of digoxin. No dose adjustment is required.

PDE5 Inhibitors

Co-administration of Silodosin with a single dose of 100 mg sildenafil or 20 mg tadalafil was evaluated in a placebo-controlled clinical study that included 24 healthy male subjects, 45 to 78 years of age. Orthostatic vital signs were monitored in the 12-hour period following concomitant dosing. During this period, the total number of positive orthostatic test results was greater in the group receiving Silodosin plus a PDE5 inhibitor compared with Silodosin alone. No events of symptomatic orthostasis or dizziness were reported in subjects receiving Silodosin with a PDE5 inhibitor (mentioned in sections 4.4 & 4.5 of SmPC).

Other Concomitant Drug Therapy

Antihypertensive

The pharmacodynamic interactions between Silodosin and antihypertensive have not been rigorously investigated in a clinical study. However, approximately one-third of the patients in clinical studies used concomitant antihypertensive medications with Silodosin. The incidence of dizziness and orthostatic hypotension in these patients was higher than in the general Silodosin population (4.6% versus 3.8% and 3.4% versus 3.2%, respectively). Exercise caution during concomitant use with antihypertensive and monitor patients for possible adverse events (mentioned in sections 4.4 & 4.5 of SmPC).

Metabolic Interactions

In vitro data indicate that Silodosin does not have the potential to inhibit or induce cytochrome P450 enzyme systems.

Food Interactions

The effect of a moderate fat, moderate calorie meal on Silodosin pharmacokinetics was variable and decreased Silodosin maximum plasma concentration (C_{max}) by approximately 18 to 43% and exposure (AUC) by 4 to 49% across three different studies. Safety and efficacy clinical trials for Silodosin were always conducted in the presence of food intake. Patients should be instructed to take Silodosin with a meal to reduce risk of adverse events.

Table 1 Adverse Reactions Occurring in ≥ 2% of Patients in 12-week, Placebo-Controlled Clinical Trials

Adverse Reactions	SILODOSIN N= 466 n (%)	Placebo N= 457 n (%)
Retrograde Ejaculation	131 (28.1)	4 (0.9)
Dizziness	15 (3.2)	5 (1.1)
Diarrhea	12 (2.6)	6 (1.3)
Orthostatic Hypotension	12 (2.6)	7 (1.5)
Headache	11 (2.4)	4 (0.9)
Nasopharyngitis	11 (2.4)	10 (2.2)
Nasal Congestion	10 (2.1)	1 (0.2)

In the two 12-week, placebo-controlled clinical trials, the following adverse events were reported by between 1% and 2% of patients receiving Silodosin and occurred more frequently than with placebo: insomnia, PSA increased, sinusitis, abdominal pain, asthenia, and rhinorrhea. One case of syncope in a patient taking prazosin concomitantly and one case of priapism were reported in the Silodosin treatment group.
In a 9-month open-label safety study of Silodosin, one case of Intraoperative Floppy Iris Syndrome (IFIS) was reported.

Post Marketing Experience

The following adverse reactions have been identified during post approval use of Silodosin. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure:
Skin and subcutaneous tissue disorders: *toxic skin eruption, purpura, skin rash, pruritus, and urticarial*
Hepatobiliary disorders: *jaundice, impaired hepatic function associated with increased transaminase values*
Immune system disorders: *allergic-type reactions, not limited to skin reactions including swollen tongue and pharyngeal edema resulting in serious outcomes*

OVERDOSE AND TREATMENT

Silodosin was evaluated at doses of up to 48 mg/day in healthy male subjects. The dose-limiting adverse event was postural hypotension.
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.

STORE AT TEMPERATURES BELOW 30°C. PROTECT FROM LIGHT AND MOISTURE.

CAUTION

Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

AVAILABILITY

Silodosin (Ureleve®) 2mg Capsule in Alu/Alu Blister Pack x 10's, Box of 30's
Silodosin (Ureleve®) 4mg Capsule in Alu/Alu Blister Pack x 10's, Box of 30's
Silodosin (Ureleve®) 8mg Capsule in Alu/Alu Blister Pack x 10's, Box of 30's

FOR SUSPECTED ADVERSE DRUG REACTION, REPORT TO THE FDA: www.fda.gov.ph.
Seek medical attention immediately at the first sign of any adverse drug reaction.

Registration No.: 2 mg - DR-XY47994
Registration No.: 4 mg - DR-XY48772
Registration No.: 8 mg - DR-XY48486

Date of First Authorization/Renewal of the Authorization :
2 mg - April 19, 2022
4 mg - June 9, 2023
8 mg - September 12, 2023

Date of Revision of Package Insert : 0

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