SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF DRUG PRODUCT

Silorap (Silodosin) Capsules 8mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains
Silodosin…8mg

3. PHARMACEUTICAL FORM

Hard gelatin capsule with pink opaque cap and white opaque body, containing white powder.

4. CLINICAL PARTICULARS

4.1 INDICATIONS

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

4.2 DOSAGE & ADMINISTRATION

Recommended Dose
Siloget (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 Siloget (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
Siloget (Silodosin) should be taken orally once daily with a meal. Siloget (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

4.3 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).

4.4 Special warnings and special precautions for use

- 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.

4.5 Interaction with other medicaments and other forms of interaction

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 monitoired for possible adverse events. Silodosin can potentially cause symptomatic hypotension

4.6 Use in Pregnancy and Lactation

Pregnancy & Nursing Mothers
Silodosin is not indicated nor recommended for use in women.

4.7 Undesirable effects

Very Common
Ejaculatory disorders, including retrograde ejaculation and an ejaculation.

Common
Dizziness, orthostatic hypotension, nasal congestion and diarrhoea.

Uncommon
Libido decreased, tachycardia, hypotension, nausea, dry mouth, abnormal liver function tests, skin rash, pruritus, urtricaria, 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.

4.8 Overdose
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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

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.

5.2 Pharmacokinetic properties

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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Mannitol
- Starch 1500 (Partially Pregelatinized)
- Sodium Lauryl Sulfate
- Magnesium Stearate
- Purified water
- EGC Silodosin 8mg Size "1"

6.2 Incompatibilities
None.

6.3 Shelf-life
2 years
The expiration date refers to the product correctly stored in the required conditions.

6.4 Special precautions for storage
- Do not store above 30°C.
- Protect from light and moisture.
- The expiry date refers to the product correctly stored at the required conditions.

6.5 Nature and contents of container
Silorap (Silodosin) Capsules 8mg are available in Alu-Alu blister pack of 30's (3 x 10 Capsules), packed in a printed unit carton along with the package insert.

6.6 Instructions for use/handling
- Keep out of reach of children.
- To be sold on prescription of a registered medical practitioner only.

7. MARKETING AUTHORISATION HOLDER
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