STORAGE CONDITIONS AND OTHER INFORMATION
• Keep this medicine out of the sight and reach of children.
• Do not use this medicine after the expiry date which is stated on the carton and on the blister after EXP. The expiry date refers to the last day of that month.
• Do not store above 30 °C.
• Store in the original package in order to protect from light and moisture.

PRESENTATION:
Silodact 4mg capsule is available in blister packs of 10's, 20's and 30's.
Silodact 8mg capsule is available in blister pack of 10's.

ہدایات:

- خوراک ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
- دوا کو ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر روشنی سے بچا کر خشک جگہ پر رکھیں۔
- صرف رجسٹرڈ ڈاکٹر کے نسخے پر ہی فروخت کریں۔
- بچوں کی پہنچ سے دور رکھیں۔

Manufactured by:
Kaizen Pharmaceuticals (Pvt.) Ltd.,
E-127-129, North Western Industrial Zone,
Bin Qasim, Karachi-75020, Pakistan.

Art no: 617

Silodact®

(Silodosin)

4 mg & 8 mg Capsules

سِلوڈیکٹ

سِلوڈوسِن

۴ اور ۸ ملی گرام کیپسولز

Silodact 4 mg Capsules:
Each capsule contains:
Silodosin (J.P Specs) ..... 4 mg.
Product complies as per *Innovator's Specifications.

Silodact 8 mg Capsules:
Each capsule contains:
Silodosin (J.P Specs)..... 8 mg.
Product complies as per *Innovator's Specifications.

CLINICAL PARTICULARS
Therapeutic indications
Treatment of the signs and symptoms of benign prostatic hyperplasia (BPH) in adult men.

POSOLOGY AND METHOD OF ADMINISTRATION
Posology
The recommended dose is one capsule of Silodact 8 mg daily. For special patient populations, one capsule of Silodact 4 mg daily is recommended.

• 8 mg capsules taken orally once daily with a meal.
• 4 mg capsules taken orally once daily with a meal for those with moderate renal impairment [Creatinine Clearance (CCr) 30-50 mL/min].

For Oral use
The capsule should be taken with food, preferably at the same time every day.

Missed dose
Take the missed dose with a meal as soon as you remember it. However, if it is almost time for the next dose, skip the missed dose and continue your regular dosing schedule. Do not take a double dose to make up for a missed one.

Special populations
Elderly
No dose adjustment is required in the elderly.

Renal impairment
No dose adjustment is required for patients with mild renal impairment (CLCR ≥ 50 to ≤ 80 mL/min). A starting dose of 4 mg once daily is recommended in patients with moderate renal impairment (CLCR ≥ 30 to < 50 mL/min), which may be increased to 8 mg once daily after one week of treatment, depending on the individual patient's response. The use in patients with severe renal impairment (CLCR < 30 mL/min) is not recommended.

Hepatic impairment
No dose adjustment is required for patients with mild to moderate hepatic impairment.

Paediatric population
There is no relevant use of Silodosin.

METHOD OF ADMINISTRATION
Oral administration.
The capsule should be taken with food, preferably at the same time every day.

CONTRAINDICATIONS
• Hypersensitivity.
• Severe renal impairment (CrCl <30 mL/min).
• Severe hepatic impairment (Child-Pugh Score >10) Concomitant strong CYP3A4 inhibitors or P-glycoprotein inhibitors.

Special warnings and precautions for use:
Orthostatic Effects
Postural hypotension, with or without symptoms (e.g., dizziness) may develop when beginning SILODACT 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.
Renal Impairment
In a clinical pharmacology study, plasma concentrations (AUC and Cmax) 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 SILODACT should be reduced to 4 mg in patients with moderate renal impairment. Exercise caution and monitor such patients for adverse events.
Hepatic Impairment
SILODACT has not been tested in patients with severe hepatic impairment, and therefore, should not be prescribed to such patients.
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 SILODACT to rule out the presence of carcinoma of the prostate.

Drug Interactions:
Some products that may interact with this drug include: other alpha blocker drugs (such as prazosin, terazosin). If you are also taking a drug to treat erectile dysfunction-ED or pulmonary hypertension (such as sildenafil, tadalafil), your blood pressure may get too low which can lead to dizziness or fainting.

Other medications can affect the removal of silodosin from your body, which may affect how silodosin works. Examples include azole antifungals . (suchas itraconazole, ketoconazole), boceprevir, clarithromycin,cobicistat, cyclosporine, HIV protease inhibitors (such as lopinavir, ritonavir), ribociclib, among others.

Fertility, pregnancy and lactation
Pregnancy/breast-feeding:
Not applicable as silodosin is intended for male patients only.

Fertility:
In clinical studies, the occurrence of ejaculation with reduced or no semen has been observed during treatment with silodosin due to the pharmacodynamic properties of silodosin.
Before starting treatment, the patient should be informed that this effect may occur, temporarily affecting male fertility.

Effects on ability to drive and use machines
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.

SIDE EFFECTS:
The more common side effects that can occur with silodosin include:
• Dizziness
• Diarrhea
• Orthostatic hypotension (low blood pressure when you stand up after sitting or lying down)
• Headache
• Retrograde ejaculation (occurs when semen enters the bladder instead of out the tip of the penis)
• common cold
• Stuffy nose
• Mild side effects may disappear within a few days or a couple of weeks. Talk to your doctor or pharmacist if they're more severe or don't go away.

Overdose
Silodosin was evaluated at doses of up to 48 mg/day in healthy male subjects.

PHARMACOLOGICAL PROPERTIES
Pharmacodynamic properties
Pharmacotherapeutic group: Urologicals, alpha-adrenoreceptor antagonists

Mechanism of action
Silodosin is highly selective for α1A-adrenoreceptors that are primarily located in the human prostate, bladder base, bladder neck, prostatic capsule and prostatic urethra. Blockade of these α1A-adrenoreceptors causes smooth muscle in these tissues to relax, thus decreasing bladder outlet resistance, without affecting detrusor smooth muscle contractility. This causes an improvement of both storage (irritative) and voiding (obstructive) symptoms (Lower urinary tract symptoms, LUTS) associated with benign prostatic hyperplasia. Silodosin has a substantially lower affinity for the α1B-adrenoreceptors that are primarily located in the cardiovascular system. It has been demonstrated in vitro that the α1A:α1B binding ratio of silodosin (162:1) is extremely high.

Pharmacokinetics:
Absorption/Bioavailability:
Silodosin administered orally is well absorbed and absorption is dose proportional. The absolute bioavailability is approximately 32%. An in vitro study with Caco-2 cells showed that silodosin is a substrate for P-glycoprotein. Food decreases Cmax by approximately 30%, increases tmax by approximately 1 hour and has little effect on AUC. In healthy male subjects of the target age range (n = 16, mean age 55 ± 8 years) after once-a-day oral administration of 8 mg immediately after breakfast for 7 days, the following pharmacokinetic parameters were obtained: Cmax 87 ± 51 ng/mL (sd), tmax 2.5 hours (range 1.0-3.0), AUC 433 ± 286 ng h/mL.

Distribution
Protein binding of silodosin glucuronide is 91%.

Protein Binding
Silodosin has a volume of distribution of 0.81 L/kg and is 96.6% bound to plasma proteins. It does not distribute into blood cells

Metabolism
Silodosin undergoes extensive metabolism through glucuronidation (UGT2B7), alcohol and aldehyde dehydrogenase and oxidative pathways, mainly CYP3A4. The main metabolite in plasma, the glucuronide conjugate of silodosin (KMD-3213G), that has been shown to be active in vitro, has an extended half-life (approximately 24 hours) and reaches plasma concentrations approximately four times higher than those of silodosin. In vitro data indicate that silodosin does not have the potential to inhibit or induce cytochrome P450 enzyme systems.

Elimination
Following oral administration of 14C-labelled silodosin, the recovery of radioactivity after 7 days was approximately 33.5% in urine and 54.9% in faeces. Body clearance of silodosin was approximately 0.28 L/h/kg. Silodosin is excreted mainly as metabolites, very low amounts of unchanged drug are recovered in urine. The terminal half-life of parent drug and its glucuronide is approximately 11 hours and 18 hours, respectively.

Pharmacokinetics in special populations
Age, gender and ethnicity
Exposure to silodosin and its main metabolites does not change significantly with age, even in subjects of age over 75 years.

Hepatic impairment
The pharmacokinetics of silodosin in patients with severe hepatic impairment has not been studied.

Renal impairment
In patients with severe renal impairment administration of Silodosin is not recommended.

Special precautions for storage
Store in the original package in order to protect from moisture.