SILDAT™ Capsule
(Silodosin)

QUALITATIVE AND QUANTITATIVE COMPOSITION

SILDAT™ Capsule 4mg
Each capsule contains:
Silodosin MS..... 4mg

SILDAT™ Capsule 8mg
Each capsule contains:
Silodosin MS..... 8mg

PHARMACEUTICAL FORM
Capsules

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, 8mg daily.

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

Hepatic Impairment:
No dose adjustment is required for patients with mild to moderate hepatic impairment. As no data are available, the use in patients with severe hepatic impairment is not recommended

Elderly patients:
No dose adjustment is required in the elderly

Paediatric patients:
There is no relevant use of silodosin in the paediatric population for the indication of benign prostatic hyperplasia (BPH).

METHOD OF ADMINISTRATION:
Oral use. The capsule should be taken with food, preferably at the same time every day. The capsule should not be broken or chewed but swallowed whole, preferably with a glass of water.

CONTRAINDICATIONS:
Hypersensitivity to the active substance or to any of the excipients.

SPECIAL WARNING AND PRECAUTIONS FOR USE:
Intraoperative Floppy Iris Syndrome (IFIS):
IFIS (a variant of small pupil syndrome) has been observed during cataract surgery in some patients on α1-blockers or previously treated with α1-blockers. This may lead to increased procedural complications during the operation.

The initiation of therapy with silodosin is not recommended in patients for whom cataract surgery is scheduled. Discontinuing treatment with an α1-blocker 1-2 weeks prior to cataract surgery has been recommended, but the benefit and duration of stopping the therapy prior to cataract surgery has not yet been established.

During pre-operative assessment, eye surgeons and ophthalmic teams should consider whether patients scheduled for cataract surgery are being or have been treated with silodosin, in order to ensure that appropriate measures will be in place to manage IFIS during surgery.

Orthostatic Effects:
The incidence of orthostatic effects with silodosin is very low. However, a reduction in blood pressure can occur in individual patients, leading in rare cases to syncope. At the first signs of orthostatic hypotension (such as postural dizziness), the patient should sit or lie down until the symptoms have disappeared. In patients with orthostatic hypotension, treatment with silodosin is not recommended.

Renal impairment:
The use of silodosin in patients with severe renal impairment (CrCl <30 ml/min) is not recommended.

Hepatic impairment:
Since no data are available in patients with severe hepatic impairment, the use of silodosin in these patients is not recommended.

Carcinoma of the prostate:
Since BPH and prostate carcinoma may present the same symptoms and can co-exist, patients thought to have BPH should be examined prior to starting therapy with silodosin, to rule out the presence of carcinoma of the prostate. Digital rectal examination and, when necessary, determination of prostate specific antigen (PSA) should be performed before treatment and at regular intervals afterwards.

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.

Sodium:
This medicinal product contains less than 1 mmol sodium (23mg) per capsule, that is to say essentially 'sodium-free'.

INTERACTION WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS:
Silodosin is metabolised extensively, mainly via CYP3A4, alcohol dehydrogenase and UGT2B7. Silodosin is also a substrate for P-glycoprotein. Substances that inhibit (such as ketoconazole, itraconazole, ritonavir or cyclosporine) or induce (such as rifampicin, barbiturates, carbamazepine, phenytoin) these enzymes and transporters may affect the plasma concentrations of silodosin and its active metabolite.

Alpha-blockers:
There is inadequate information about the safe use of silodosin in association with other α-adrenoreceptor antagonists. Consequently, the concomitant use of other α-adrenoreceptor antagonists is not recommended.

CYP3A4 inhibitors:
Concomitant use with potent CYP3A4 inhibitors (such as ketoconazole, itraconazole, ritonavir or cyclosporine) is not recommended. When silodosin was co-administered with a CYP3A4 inhibitor of moderate potency such as diltiazem, an increase in silodosin AUC of approximately 30% was observed, but C_{max} and half-life were not affected. This change is clinically not relevant and no dose adjustment is required.

PDE-5 inhibitors:
Minimal pharmacodynamic interactions have been observed between silodosin and maximum doses of sildenafil or tadalafil. Patients taking PDE-5 inhibitors concomitantly with silodosin should be monitored for possible adverse reactions.

Antihypertensive:
Caution should be exercised when starting concomitant use with antihypertensives and patients should be monitored for possible adverse reactions.

Digoxin:
No dose adjustment is required.

FERTILITY, PREGNANCY AND LACTATION:
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.

Pregnancy and breast-feeding:
Not applicable as silodosin is intended for male patients only.

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.

UNDESIRABLE EFFECTS:
The following adverse reactions have been identified during post approval use of silodosin. Since 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.

Intraoperative Floppy Iris Syndrome (IFIS):
IFIS has been reported during cataract surgery.

OVERDOSE:
Silodosin was evaluated at doses of up to 48mg/day in healthy male subjects. The dose-limiting adverse reaction was postural hypotension. If ingestion is recent, induction of vomiting or gastric lavage may be considered.
Should overdose of silodosin lead to hypotension, cardiovascular support has to be provided. Dialysis is unlikely to be of significant benefit since silodosin is highly (96.6%) protein bound.

PHARMACOLOGICAL PROPERTIES

PHARMACODYNAMICS PROPERTIES:
Therapeutic Classification & ATC Codes:

Pharmacotherapeutic group: Urologicals, alpha-adrenoreceptor antagonists.

ATC code: G04CA04.

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.

PHARMACOKINETIC PROPERTIES:
Absorption:
Silodosin administered orally is well absorbed and absorption is dose proportional. The absolute bioavailability is approximately 32%. Food decreases Cmax by approximately 30%, increases tmax by approximately 1 hour and has little effect on AUC.

Distribution:
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. Protein binding of silodosin glucuronide is 91%.

Biotransformation:
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

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.

SHELF LIFE
See expiry on the pack.

AVAILABILITY
SILDAT™ capsule 4mg in a pack of 10's
SILDAT™ capsule 8mg in a pack of 10's

INSTRUCTIONS
Dosage: As advised by the physician.
To be sold on the prescription of registered medical practitioner.
Keep out of reach of children.
Avoid exposure to heat, light and humidity.
Store between 15 to 30°C.
Improper storage may deteriorate the medicine.

سِلڈیٹ™ کیپسول
(سائلوڈوسن)

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
صرف رجسٹرڈ ڈاکٹر کے نسخے کے مطابق فروخت کریں۔
بچوں کی پہنچ سے دور رکھیں۔
دوا کو دھوپ، گرمی اور نمی سے محفوظ ۱۵ سے ۳۰ ڈگری سینٹی گریڈ
کے درمیان میں رکھیں ورنہ دوا خراب ہو جائیگی۔

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