1.3 PRODUCT INFORMATION

1.3.1 Summary of product Characterstics (SmPC)

The Summary of Product Characteristics has been enclosed in the following pages.

SUMMARY OF PRODUCT CHARACTERSTICS

Summary of product characteristics

SILODOSIN CAPSULES 4 mg & 8 mg

1. NAME OF THE MEDICINAL PRODUCT

Silodosin capsules 4 mg & 8 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each hard capsule contains silodosin 4 mg , 8 mg.

For the full list of excipients, see section 6.1.

3.PHARMACEUTICAL FORM

Hard gelatin capsule.

4 mg: White to off white color granular powder was filled in size "3" hard gelatin capsules with grey color body and red color cap..

8 mg: White to off white color granular powder was filled in size "2" hard gelatin capsules with golden yellow color body and golden yellow color cap.

4.CLINICAL PARTICULARS

4.1 Therapeutic indications

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

4.2 Posology and method of administration

Posology

The recommended dose is one capsule of Silodosin 8 mg daily. For special patient populations, one capsule of Silodosin 4 mg daily is recommended (see below).

Elderly

No dose adjustment is required in the elderly (see section 5.2).

Renal impairment

No dose adjustment is required for patients with mild renal impairment (CL_{CR} ≥50 to ≤80 ml/min).A starting dose of 4 mg once daily is recommended in patients with moderate renal impairment (CL_{CR} ≥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 (CL_{CR} <30 ml/min) is not recommended (see sections 4.4 and 5.2).

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 (see sections 4.4 and 5.2).

Paediatric population

There is no relevant use of Silodosin in the paediatric population in the indication.

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.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings 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 α_1-blockers or previously treated with α_1-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 α_1-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 (CL_{CR} <30 ml/min) is not recommended (see sections 4.2 and 5.2).

Hepatic impairment

Since no data are available in patients with severe hepatic impairment, the use of silodosin in these patients is not recommended (see sections 4.2 and 5.2).

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 (see section 4.8).

4.5 Interaction with other medicinal products and other forms of interaction

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

In an interaction study, a 3.7-fold increase in maximum silodosin plasma concentrations and a 3.1-fold increase in silodosin exposure (i.e. AUC) were observed with concurrent administration of a potent CYP3A4 inhibitor (ketoconazole 400 mg). 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. In a placebo-controlled study in 24 subjects 45-78 years of age receiving silodosin, the co-administration of sildenafil 100 mg or tadalafil 20 mg induced no clinically meaningful mean decreases in systolic or diastolic blood pressure, as assessed by orthostatic tests (standing *versus* supine). In the subjects over 65 years, the mean decreases at the various time points were between 5 and 15 mmHg (systolic) and 0 and 10 mmHg (diastolic). Positive orthostatic tests were only slightly more common during co-administration; however, no symptomatic orthostasis or dizziness occurred. Patients taking PDE-5 inhibitors concomitantly with silodosin should be monitored for possible adverse reactions.

Antihypertensives

In the clinical study program, many patients were on concomitant antihypertensive therapy (mostly agents acting on the renin-angiotensin system, beta-blockers, calcium antagonists and diuretics) without experiencing an increase in the incidence of orthostatic hypotension. Nevertheless, caution should be exercised when starting concomitant use with antihypertensives and patients should be monitored for possible adverse reactions.

Digoxin

Steady state levels of digoxin, a substrate of P-glycoprotein, were not significantly affected by co-administration with silodosin 8 mg once daily. No dose adjustment is required.

4.6 Fertility, pregnancy and lactation

Pregnancy and 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 (see section 4.8), due to the pharmacodynamic properties of silodosin. Before starting treatment, the patient should be informed that this effect may occur, temporarily affecting male fertility.

4.7 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.

4.8 Undesirable effects

Summary of the safety profile

The safety of silodosin has been evaluated in four Phase II-III double-blind controlled clinical studies (with 931 patients receiving silodosin 8 mg once daily and 733 patients receiving placebo) and in two long-term open-label extension phase studies. In total, 1,581 patients have received silodosin at a dose of 8 mg once daily, including 961 patients exposed for at least 6 months and 384 patients exposed for 1 year. The most frequent adverse reactions reported with silodosin in placebo controlled clinical studies and during long-term use were ejaculatory disorders such as retrograde ejaculation and anejaculation (ejaculatory volume reduced or absent), with a frequency of 23 %. This may temporarily affect male fertility. It is reversible within a few days upon discontinuation of treatment (see section 4.4).

Tabulated list of adverse reactions

In the table below, adverse reactions reported in all clinical studies and in the worldwide post-marketing experience for which a reasonable causal relationship exists are listed by MedDRA system organ class and frequency: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000), not known (cannot be estimated from available data). Within each frequency grouping the observed adverse reactions are presented in order of decreasing seriousness.

	Very common	Common	Uncommon	Rare	Very rare	Not known
Immune system disorders					Allergic-type reactions including facial swelling, swollen tongue and pharyngeal oedema[1]	
Psychiatric disorders			Libido decreased			
Nervous system disorders		Dizziness		Syncope Loss of consciousness[1]		

Cardiac disorders			Tachycardia[1]	Palpitations[1]		
Vascular disorders		Orthostatic hypotension	Hypotension[1]			
Respiratory, thoracic and mediastinal disorders		Nasal congestion				
Gastrointestinal disorders		Diarrhoea	Nausea Dry mouth			
Hepatobiliary disorders			Abnormal liver function tests[1]			
Skin and subcutaneous tissue disorders			Skin rash[1], Pruritus[1] Urticaria[1] Drug eruption[1]			
Reproductive system and breast disorders	Ejaculatory disorders, including retrograde ejaculation, anejaculation		Erectile dysfunction			
Injury, poisoning and procedural complication						Intraoperative Floppy Iris Syndrome

[1] - adverse reactions from spontaneous reporting in the worldwide post-marketing experience (frequencies calculated from events reported in Phase I-IV clinical trials and non-interventional studies).

Description of selected adverse reactions

Orthostatic hypotension

The incidence of orthostatic hypotension in placebo-controlled clinical studies was 1.2 % with silodosin and 1.0 % with placebo. Orthostatic hypotension may occasionally lead to syncope (see section 4.4).

Intraoperative Floppy Iris Syndrome (IFIS)

IFIS has been reported during cataract surgery (see section 4.4).

4.9 Overdose

Silodosin was evaluated at doses of up to 48 mg/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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Urologicals, alpha-adrenoreceptor antagonists, ATC code: G04CA04.

Mechanism of action

Silodosin is highly selective for α_{1A}-adrenoreceptors that are primarily located in the human prostate,bladder base, bladder neck, prostatic capsule and prostatic urethra. Blockade of these α_{1A}-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 α_{1B}-adrenoreceptors that are primarily located in the cardiovascular system. It has been demonstrated *in vitro* that the α_{1A}:α_{1B} binding ratio of silodosin (162:1) is extremely high.

Clinical efficacy and safety

In a Phase II dose-finding, double-blind, placebo-controlled clinical study with silodosin 4 or 8 mg once daily, a greater improvement in American Urologic Association (AUA) symptom index score was observed with silodosin 8 mg (-6.8±5.8, n=90; p=0.0018) and silodosin 4 mg (-5.7±5.5, n=88; p=0.0355) as compared to placebo (-4.0±5.5, n=83).

Over 800 patients with moderate to severe symptoms of BPH (International Prostate Symptom Score, IPSS, baseline value ≥13) received silodosin 8 mg once daily in two Phase III placebo-controlled clinical studies conducted in the United States and in one placebo- and active-controlled clinical study conducted in Europe. In all studies, patients who did not respond to placebo during a 4-week placebo run-in phase were randomised to receive the study treatment. In

all studies, patients treated with silodosin had a greater decrease in both storage (irritative) and voiding (obstructive) symptoms of BPH as compared to placebo as assessed after 12 weeks of treatment. Data observed in the Intent-to-treat populations of each study are shown below:

Study	**Treatment arm**	**No. of patients**	**IPSS Total score**			**IPSS Irritative symptoms**		**IPSS Obstructive symptoms**	
			Baseline value (±SD)	Change from baseline	Difference (95 % CI) vs placebo	Change from baseline	Difference (95 % CI) vs placebo	Change from baseline	Difference (95 % CI) vs placebo
US-1	Silodosin	233	22 ± 5	-6.5	-2.8* (-3.9, -1.7)	-2.3	-0.9* (-1.4, -0.4)	-4.2	-1.9* (-2.6, -1.2)
	Placebo	228	21± 5	-3.6		-1.4		-2.2	
US-2	Silodosin	233	21 ± 5	-6.3	-2.9* (-4.0, -1.8)	-2.4	-1.0* (-1.5, -0.6)	-3.9	-1.8* (-2.5, -1.1)
	Placebo	229	21 ± 5	-3.4		-1.3		-2.1	
Europe	Silodosin	371	19 ± 4	-7.0	-2.3* (-3.2, -1.4)	-2.5	-0.7° (-1.1, -0.2)	-4.5	-1.7* (-2.2, -1.1)
	Tamsulosin	376	19 ± 4	-6.7	-2.0* (-2.9, -1.1)	-2.4	-0.6° (-1.1, -0.2)	-4.2	-1.4* (-2.0, -0.8)
	Placebo	185	19 ± 4	-4.7		-1.8		-2.9	

* p<0.001 vs Placebo; ° p =0.002 vs Placebo

In the active-controlled clinical study conducted in Europe, silodosin 8 mg once daily was shown to be non inferior to tamsulosin 0.4 mg once daily: the adjusted mean difference (95 % CI) in the IPSS Total Score between treatments in the per-protocol population was 0.4 (-0.4 to 1.1). The responder rate (i.e. improvement in the IPSS total score by at least 25 %) was significantly higher in the silodosin (68 %) and tamsulosin group (65 %), as compared to placebo (53 %).

In the long-term open-label extension phase of these controlled studies, in which patients received silodosin for up to 1 year, the symptom improvement induced by silodosin at week 12 of treatment was maintained over 1 year.

In a Phase IV clinical trial performed in Europe, with a mean baseline IPSS total score of 18.9 points, 77.1 %were responders to silodosin (as assessed by a change from baseline in the IPSS total score of at least 25 %). Approximately half of the patients reported an improvement in the most bothersome symptoms complained at baseline by the patients (i.e. nocturia, frequency, decreased stream, urgency, terminal dribbling and incomplete emptying), as assessed by the ICS-male

questionnaire.

No significant reduction in supine blood pressure was observed in all clinical studies conducted with silodosin.

Silodosin 8 mg and 24 mg daily had no statistically significant effect on ECG intervals or cardiac repolarisation relative to placebo.

Paediatric population

The European Medicines Agency has waived the obligation to submit the results of studies with Silodosin in all subsets of the paediatric population in BPH (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

The pharmacokinetics of silodosin and its main metabolites have been evaluated in adult male subjects with and without BPH after single and multiple administrations with doses ranging from 0.1 mg to 48 mg per day. The pharmacokinetics of silodosin is linear throughout this dose range.

The exposure to the main metabolite in plasma, silodosin glucuronide (KMD-3213G), at steady-state is about 3-fold that of the parent substance. Silodosin and its glucuronide reach steady-state after 3 days and 5 days of treatment, respectively.

Absorption

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 C_{max} by approximately 30 %, increases t_{max} 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: C_{max} 87±51 ng/ml (sd), t_{max} 2.5 hours (range 1.0-3.0), AUC 433±286 ng • h/ml.

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

Elimination

Following oral administration of ^{14}C-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.

Special populations

Elderly

Exposure to silodosin and its main metabolites does not change significantly with age, even in subjects of age over 75 years.

Paediatric population

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

Hepatic impairment

In a single-dose study, the pharmacokinetics of silodosin was not altered in nine patients with moderate hepatic impairment (Child-Pugh scores 7 to 9), compared to nine healthy subjects. Results from this study should be interpreted with caution, since enrolled patients had normal biochemistry values, indicating normal metabolic function, and they were classified as having moderate liver impairment based on ascites and hepatic encephalopathy.

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

Renal impairment

In a single-dose study, exposure to silodosin (unbound) in subjects with mild (n=8) and moderate renal impairment (n=8) resulted, on average, in an increase of C_{max} (1.6-fold) and AUC (1.7-fold) relative to subjects with normal renal function (n=8). In subjects with severe renal impairment (n=5) 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.

Plasma level monitoring in a Phase III clinical study showed that levels of total silodosin after 4 weeks of treatment did not change in patients with mild impairment (n=70), compared to patients with normal renal function (n=155), while the levels were doubled on average in patients with moderate impairment (n=7).

A review of safety data of patients enrolled in all clinical studies does not indicate that mild renal impairment (n=487) poses an additional safety risk during silodosin therapy (such as an increase in dizziness or orthostatic hypotension) as compared to patients with normal renal function (n=955). Accordingly, no dose adjustment is required in patients with mild renal impairment. Since only limited experience exists in patients with moderate renal impairment (n=35), a lower starting dose of 4 mg is recommended. In patients with severe renal impairment administration of Silodosin is not recommended.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, carcinogenic, mutagenic and teratogenic potential. Effects in animals (affecting the thyroid gland in rodents) were observed only at exposures considered sufficiently in excess of the maximum human exposure, indicating little relevance to clinical use.

In male rats, decreased fertility was observed from exposures which were approximately twice the exposure at the maximum recommended human dose. The observed effect was reversible.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule contents

Mannitol , Pregelatinised starch ,Sodium lauryl sulphate , Magnesium Stearate

Capsule shell contents

4 mg: size “3” hard gelatin capsules with grey color body and red color cap.

Composition: Gelatin, Methylparaben, Propylparaben, Sodium Lauryl Sulphate, Purified Water, Brilliant Blue, Carmoisine, Tartrazine, Titanium dioxide.

8 mg: size “2” hard gelatin capsules with golden yellow color body and golden yellow color cap.

Composition: Gelatin ,Methyl Paraben, Propyl Paraben, Sodium Lauryl Sulfate, Purified Water, Sunset yellow, Tartrazine, Titanium Dioxide.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Do not store above 30°C.

6.5 Nature and contents of container

10's Alu – Alu strip pack.

6.6 Special precautions for disposal

No special requirements.

7. Manufactured by:

MSN LABORATORIES PRIVATE LIMITED,

(Formulations Division),

Plot No: 42, Anrich Industrial Estate,

IDA, Bollaram, Sangareddy District,

Telangana, India.

1.3.2 Labelling (outer & inner labels)

The artworks of container label, carton & Pack Insert for SILOTRIF 4 (Silodosin Capsules 4 mg) are enclosed in the following pages.

Harmonization

Botswana, Nigeria, Rwanda, Ethiopia, Zambia, Malawi, Tanzania, Uganda, Burundi, Mauritius, Madagascar, Namibia, IVC.

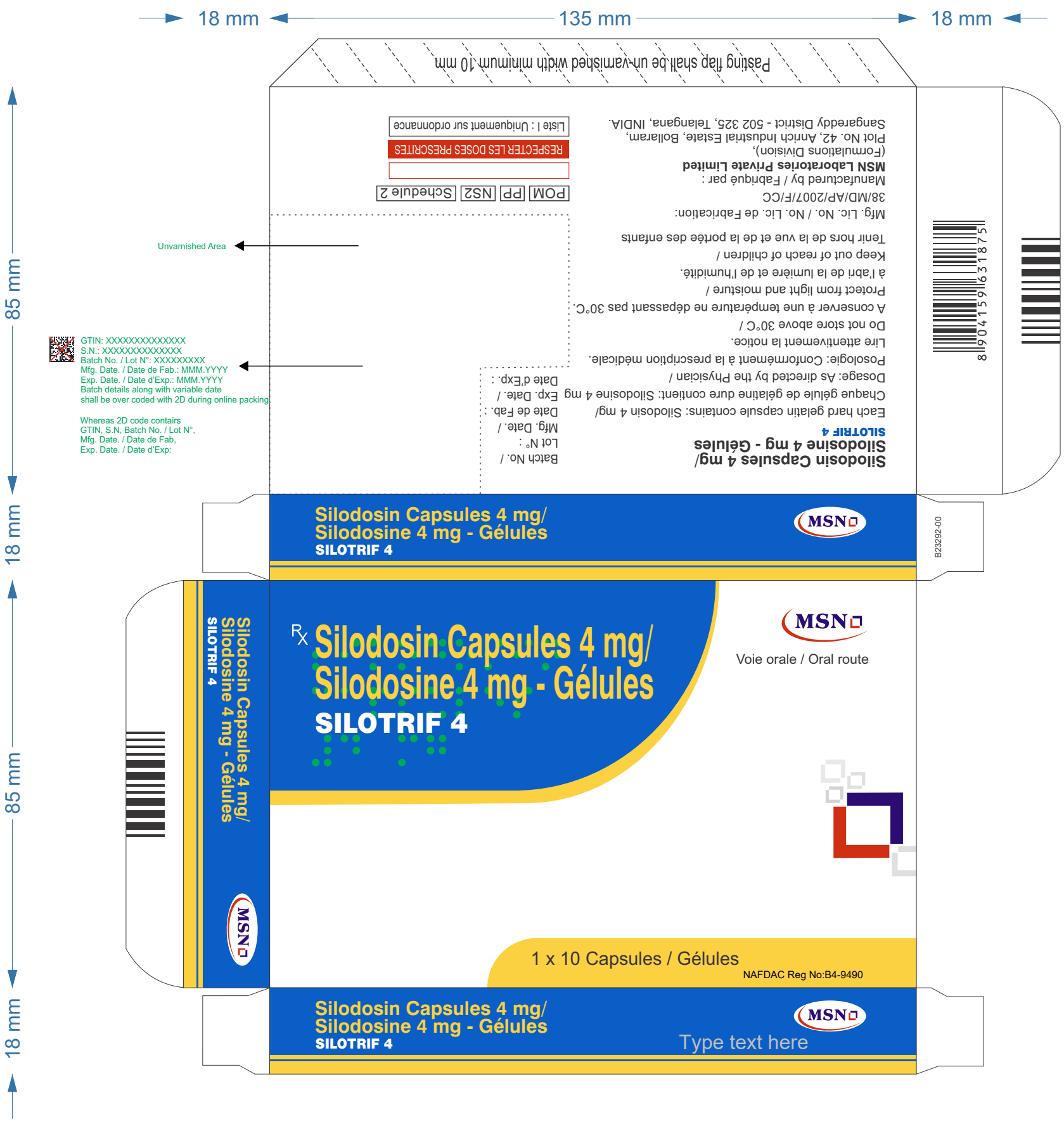
Strip Size : 130 x 80 mm
Foil width : 262 mm

MSN LABORATORIES PRIVATE LIMITED — PACKAGING DEVELOPMENT

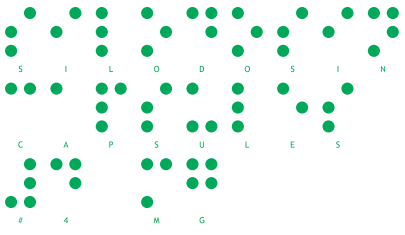
Artwork Information		Specification for Printed Foil	
		Test	Specification
Brand Name	Silotrif 4	Description	Printed Soft tempered aluminium foil with LDPE coating on the sealing side.
Generic Name	Silodosin Capsules 4 mg		
Pack Style	10's	Thickness of Aluminium	0.037 to 0.043 mm
Foil Width	262 mm	Width	262 ± 1.0 mm (261 – 263 mm)
Item Code	B12958-00	Aluminium foil GSM	108 ± 8% (99.36 - 116.64) GSM
Supersede Code	NA	VMCH Coating GSM	35 ± 8% (32.20 - 37.80) GSM
Change Part No:	–	NC Coating	NA
Version	00	Pin Holes	Nil
Date & Time	23-08-2023 / 1:48pm	Ink Adhesion Test	No Ink Lifting
Country	Harmonization Botswana, Nigeria, Rwanda, Ethiopia, Zambia, Malawi, Tanzania, Uganda, Burundi, Mauritius, Madagascar, Namibia, IVC.	Inner Core Diameter	76 ± 1 mm
Customer	NA	PRC/Non-PRC	Non-PRC (Continues text)
Font Type	Arial	Eye Mark Size	NA
Font Size (min.)	5pt	Perforation/Non-Perforation	Non-Perforation
Developed by	Sridhar	Colours	BLACK
Reviewed by	Srilakshmi		485 C

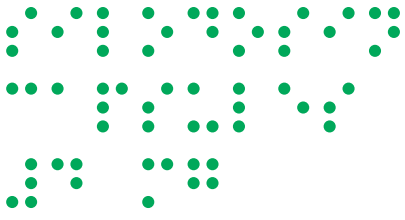
Harmonization

Botswana, Nigeria, Rwanda, Ethiopia, Zambia, Malawi, Tanzania, Uganda, Burundi, Mauritius, Madagascar, Namibia, IVC.



- Braille Text embossed not to be print



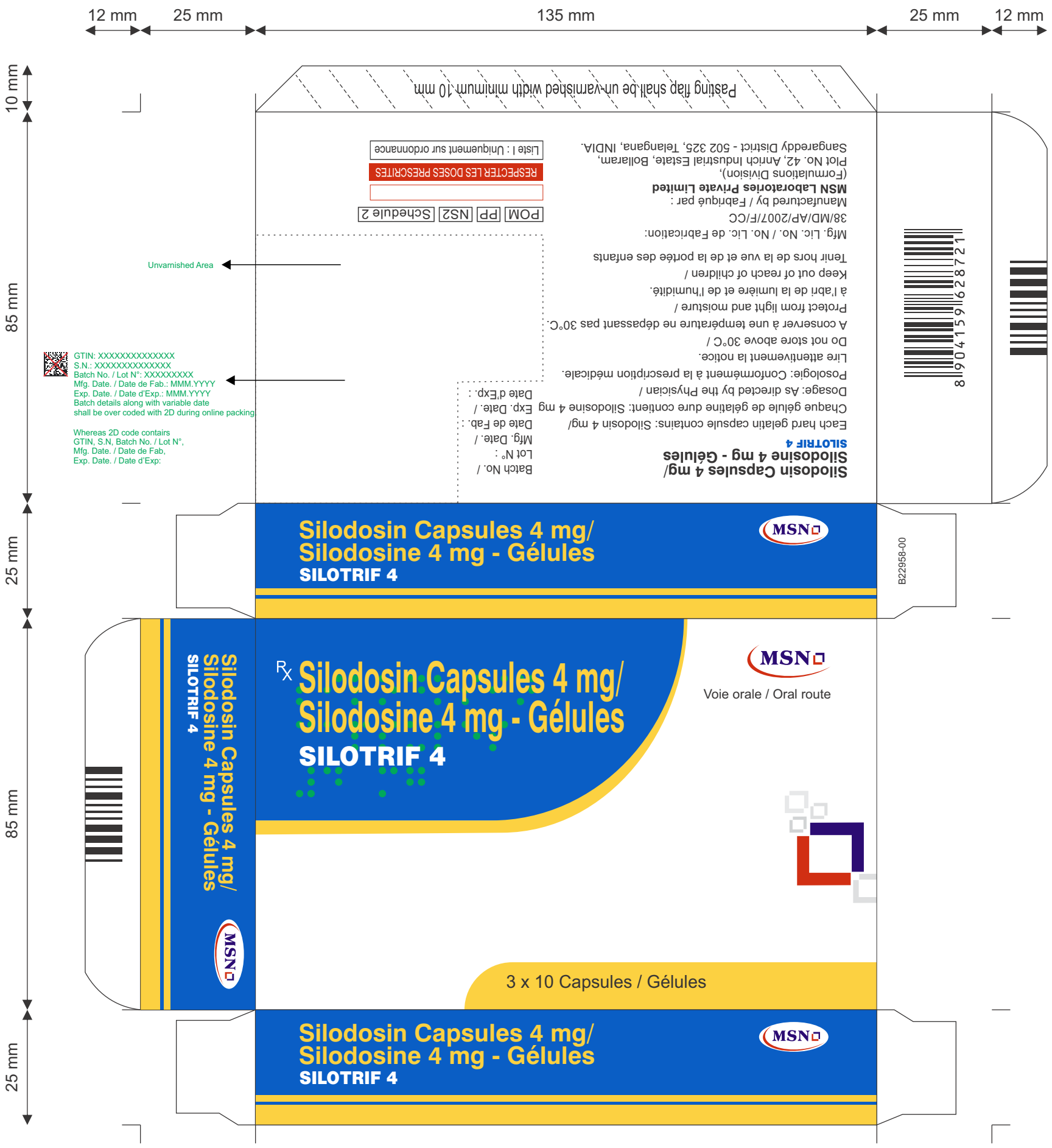


MSN LABORATORIES PRIVATE LIMITED		PACKAGING DEVELOPMENT	
Artwork Information		Specification for Printed Carton	
		Test	Specification
Brand Name	SILOTRIF 4	Substrate	Cyber XL board with reverse tuck in type
Generic Name	Silodosin Capsules 4 mg	GSM	300 ± 5%
Pack Style	10`s Pack	Varnish/Lamination	UV Varnish except over printing area
Dimensions	135 x 18 x 85 mm (LxWxH)	Mode of supply	Bundles 25's, 50's & 100's
Item Code	B23292-00	Pharmacode	4301
Supersede Code	NA	Font Type	Arial
Version	00	Font Size (min.)	7pt
Date & Time	23-08-2023 / 1:57pm	Reviewed by	Srilakshmi
Country	Harmonization Botswana, Nigeria, Rwanda, Ethiopia, Zambia, Malawi, Tanzania, Uganda, Burundi, Mauritius, Madagascar, Namibia, IVC.	Colours	PANTONE 2935C, PANTONE 485 C, PANTONE 273 C, Black, PANTONE 122 C
Customer	–		
Developed by	Sridhar		

Silodosin Capsules #4 mg

Harmonization

Botswana, Nigeria, Rwanda, Ethiopia, Zambia, Malawi, Tanzania, Uganda, Burundi, Mauritius, Madagascar, Namibia, IVC.



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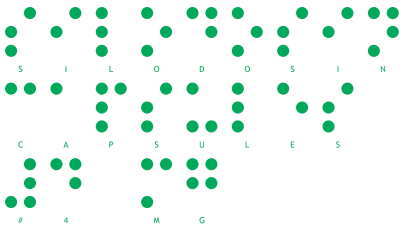
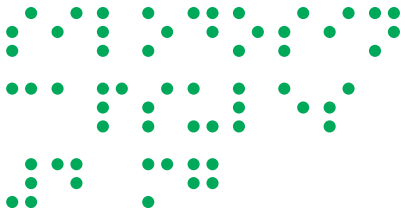




MSN LABORATORIES PRIVATE LIMITED		PACKAGING DEVELOPMENT	
Artwork Information		Specification for Printed Carton	
		Test	Specification
Brand Name	SILOTRIF 4	Substrate	Cyber XL board with reverse tuck in type
Generic Name	Silodosin Capsules 4 mg	GSM	300 ± 5%
Pack Style	30`s Pack	Varnish/Lamination	UV Varnish except over printing area
Dimensions	135 x 25 x 85 mm (LxWxH)	Mode of supply	Bundles 25's, 50's & 100's
Item Code	B22958-00	Pharmacode	3213
Supersede Code	NA	Font Type	Arial
Version	00	Font Size (min.)	7pt
Date & Time	23-08-2023 / 1:50pm	Reviewed by	Srilakshmi
Country	Harmonization Botswana, Nigeria, Rwanda, Ethiopia, Zambia, Malawi, Tanzania, Uganda, Burundi, Mauritius, Madagascar, Namibia, IVC.	Colours	PANTONE 2935C, PANTONE 485 C, PANTONE 273 C, Black, PANTONE 122 C
Customer	–		
Developed by	Sridhar		

Silodosin Capsules #4 mg

Harmonization
Botswana, Nigeria, Rwanda, Ethiopia, Zambia, Malawi, Tanzania,
Uganda, Burundi, Mauritius, Madagascar, Namibia, IVC,

470 mm

340 mm

(Silodosin Capsules 4/8 mg)
Silotrif 4/8

NAME OF THE MEDICINAL PRODUCT
Silotrif 4/8 (Silodosin Capsules 4/8 mg)

QUALITATIVE AND QUANTITATIVE COMPOSITION
Each hard gelatin capsule contains Silodosin 4 mg / 8mg

For the full list of excipients, see section pharmaceutical particulars.

PHARMACEUTICAL FORM
Hard gelatin capsules

Silodosin Capsules 4mg: White to off white color granular powder was filled in size "3" hard gelatin capsules with grey color body and red color cap.
Silodosin Capsules 8mg: White to off white color granular powder was filled in size " 2" hard gelatin capsules with golden yellow color body and golden yellow color cap.

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

DOSAGE AND ADMINISTRATION

Dosing Information
The recommended dose is 8 mg orally once daily with a meal. Patients who have difficulty swallowing pills and capsules may carefully open the SILODOSIN capsule and sprinkle the powder inside on a tablespoonful 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 (ChildPugh score > 10) and is therefore contraindicated in these patients. No dosage adjustment is needed in patients with mild or moderate hepatic impairment.

CONTRAINDICATIONS
- Severe renal impairment (CCr < 30 mL/min)
- Severe hepatic impairment (Child-Pugh score ≥ 10)
- Concomitant administration with strong Cytochrome P450 3A4 (CYP3A4) inhibitors (e.g., ketoconazole, clarithromycin, itraconazole, ritonavir)
- Patients with a history of hypersensitivity to silodosin or any of the ingredients of Silodosin capsules.

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.

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 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.

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.

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.

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. Nevertheless, exercise caution during concomitant use with antihypertensives and monitor patients for possible adverse events.

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.

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.

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.

ADVERSE REACTIONS
Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

In U.S. clinical trials, 897 patients with BPH were exposed to 8 mg Silodosin daily. This includes 486 patients exposed for 6 months and 168 patients exposed for 1 year. The population was 44 to 87 years of age, and predominantly Caucasian. Of these patients, 42.8% were 65 years of age or older and 10.7% were 75 years of age or older.

In double-blind, placebo controlled, 12-week clinical trials, 466 patients were administered Silodosin and 457 patients were administered placebo. At least one treatment-emergent adverse reaction was reported by 55.2% of Silodosin treated patients (36.8% for placebo treated). The majority (72.1%) of adverse reactions for the Silodosin treated patients (59.8% for placebo treated) were qualified by the investigator as mild. A total of 6.4% of Silodosin treated patients (2.2% for placebo treated) discontinued therapy due to an adverse reaction (treatment-emergent), the most common reaction being retrograde ejaculation (2.8%) for Silodosin treated patients. Retrograde ejaculation is reversible upon discontinuation of treatment.

Adverse Reactions observed in at least 2% of patients:
The incidence of treatment-emergent adverse reactions listed in the following table were derived from two 12-week, multicenter, double-blind, placebo-controlled clinical studies of Silodosin 8 mg daily in BPH patients. Adverse reactions that occurred in at least 2% of patients treated with Silodosin and more frequently than with placebo are shown in Table 1.

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.

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.

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 Pgp 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.

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.

Other Concomitant Drug Therapy
Antihypertensives
The pharmacodynamic interactions between silodosin and antihypertensives 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 antihypertensives and monitor patients for possible adverse events.

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 (Cmax) 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.

USE IN SPECIFIC POPULATIONS

Pregnancy
Risk Summary
Silodosin is not indicated for use in females.

Lactation
Silodosin is not indicated for use in females.

Females and Males of Reproductive Potential
Infertility
Males
Possible effects on male fertility could be observed based on findings in rats at exposures that were at least two times higher than at the MRHD (based on AUC). These findings may be reversible, and the clinical relevance is unknown.

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.

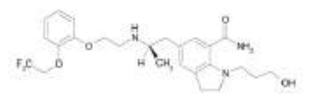
Hepatic Impairment
In a study comparing nine male patients with moderate hepatic impairment (Child-Pugh scores 7 to 9), to nine healthy male subjects, the single dose pharmacokinetics of silodosin were not significantly altered in patients with hepatic impairment. No dosing adjustment is required in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

OVERDOSAGE
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.

DESCRIPTION
Silotrif is the brand name for silodosin, 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 and the molecular formula is C25H32F3N3O4 with a molecular weight of 495.53. The structural formula of silodosin is:



Silodosin is a white to pale yellowish white powder that melts at approximately 105 to 109°C. It is very soluble in acetic acid, freely soluble in alcohol, and very slightly soluble in water. Each SILODOSIN 8 mg capsule for oral administration contains 8 mg silodosin, and the following inactive ingredients: D-mannitol, magnesium stearate, pregelatinized starch, and sodium lauryl sulfate. The size #2 hard gelatin capsules contain gelatin and titanium dioxide. Each SILODOSIN 4 mg capsule for oral administration contains 4 mg silodosin, and the following inactive ingredients: D-mannitol, magnesium stearate, pregelatinized starch, and sodium lauryl sulfate. The size #3 hard gelatin capsules contain gelatin and titanium dioxide.

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 BPH symptoms.

An in vitro study examining binding affinity of silodosin to the three subtypes of the alpha-1 adrenoreceptors (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
Pharmacotherapeutic group: Urologicals, alpha-adrenoreceptor antagonists, ATC code: G04CA04.

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 a "worst-case" scenario exposure (i.e., in the setting of concomitant renal disease or use of strong CYP3A4 inhibitors). 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. There has been no signal of Torsade de Pointes in the post-marketing experience with silodosin outside the United States.

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.

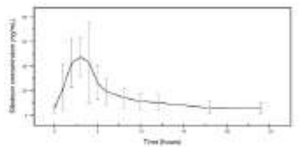
Absorption
The pharmacokinetic characteristics of silodosin 8 mg once daily were determined in a multi-dose, open-label, 7-day pharmacokinetic study completed in 19 healthy, target-aged (> 45 years of age) male subjects. Table 3 presents the steady state pharmacokinetics of this study.

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

Cmax (ng/mL)	*tmax (hours)*	t1/2 *(hours)*	*AUCss (ng•hr/mL)*
61.6 ± 27.54	2.6 ± 0.90	13.3 ± 8.07	373.4 ± 164.94

Cmax = maximum concentration, tmax = time to reach Cmax, t1/2 = elimination half-life, AUCss = 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 Cmax 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 #2) of silodosin sprinkled on applesauce compared to the product administered as an intact capsule. Based on AUC0-24 and Cmax, 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.

Elimination
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, Cmax, 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 Cmax 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 the 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 coadministered with the 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 Cmax 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 Cmax 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 coadministering 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 a 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, singlesequence, 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 Cmax 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.

NONCLINICAL TOXICOLOGY
Carcinogenesis, Mutagenesis, and Impairment of Fertility
In a 2-year oral carcinogenicity study in rats administered doses up to 150 mg/kg/day [about 8 times the exposure at the MRHD 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 9 times the exposure at the MRHD based on AUC of silodosin) and 400 mg/kg/day in females (about 72 times the exposure at the MRHD 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. Silodosin produced no evidence of mutagenic or genotoxic potential in the in vitro Ames assay, mouse lymphoma assay, unscheduled DNA synthesis assay and the in vivo mouse micronucleus assay. A weakly positive response was obtained in two in vitro Chinese Hamster Lung (CHL) tests for chromosomal aberration assays at high, cytotoxic concentrations. Treatment of male rats with silodosin for 15 days resulted in decreased fertility at the high dose of 20 mg/kg/day (about 2 times the exposure at the MRHD based on AUC) which was reversible following a two-week recovery period. No effect was observed at 6 mg/kg/day. The clinical relevance of this finding is not known. In a fertility study in female rats, the high dose of 20 mg/kg/day (about 1 to 4 times the exposure at the MRHD based on AUC) resulted in estrus cycle changes, but no effect on fertility. No effect on the estrus cycle was observed at 6 mg/kg/day. In a male rat fertility study, sperm viability and count were significantly lower after administration of 600 mg/kg/day (about 65 times the exposure at the MRHD based on AUC) for one month. Histopathological examination of infertile males revealed changes in the testes and epididymides at 200 mg/kg/day (about 30 times the exposure at the MRHD based on AUC).

PHARMACEUTICAL PARTICULARS

List of excipients
Mannitol , Pregelatinised starch , Sodium lauryl sulphate , Magnesium Stearate.

Capsule shell
4mg: Size '3' hard gelatin capsules with Grey color body and red color cap.
8mg : Size '2' hard gelatin capsules with golden yellow color body and golden yellow color cap

Incompatibilities
Not applicable.

Special precautions for storage
Do not store above 30°C. Protect from light and moisture. Keep out of reach of children.

Nature and contents of container
Alu-Alu Strip pack of 10 Capsules
Pack sizes: 1X10's, 3X10's & 10x10's
Not all pack sizes may be marketed.

Special precautions for disposal
No special requirements.

Legal Category: POM | PP | NS2 | Schedule2

B32958-00

Manufactured by :
MSN Laboratories Private Limited
(Formulations Division),
Plot No.: 42, Anrich Industrial Estate,
Bollaram, Sangareddy District -502 325,
Telangana, India.

DATE OF REVISION OF THE TEXT
May 2022

470 x 340 mm

MSN LABORATORIES PRIVATE LIMITED — PACKAGING DEVELOPMENT

Artwork Information		Specification for Printed Leaflet	
		Test	Specification
Brand Name	SILOTRIF 4 & 8	Substrate	Bible Paper
Generic Name	Silodosin Capsules 4/8 mg	GSM	40 ± 10%
Pack Style	NA	Mode of supply	Tray Pack
Dimensions	470 x 340 ± 2 mm	Pharmacode	3215
Folding Size	35 x 70 ± 2 mm	Font Type	NA
Item Code	B32958-00	Font Size (min.)	6 pt
Supersede Code	NA	Developed by	Sridhar
Version	00	Reviewed by	Srilakshmi
Date & Time	09-01-2024 / 11:15am	Colours	Black
Country	Harmonization Botswana, Nigeria, Rwanda, Ethiopia, Zambia, Malawi, Tanzania, Uganda, Burundi, Mauritius, Madagascar, Namibia, IVC,		
Customer	–		

470 mm

340 mm

Silodosine 4/8 mg - Gélules
Silotrif 4/8

Veuillez lire attentivement cette notice avant de prendre ce médicament car elle contient des informations importantes pour vous.

- Gardez cette notice. Vous pourriez avoir besoin de la relire.
- Si vous avez d'autres questions, interrogez votre médecin, votre pharmacien ou votre infirmier/ère.
- Ce médicament vous a été personnellement prescrit. Ne le donnez pas à d'autres personnes. Il pourrait leur être nocif, même si les signes de leur maladie sont identiques aux vôtres.
- Si vous ressentez un quelconque effet indésirable, parlez-en à votre médecin, votre pharmacien ou votre infirmier/ère. Ceci s'applique aussi à tout effet indésirable qui ne serait pas mentionné dans cette notice. Voir rubrique 4.

Que contient cette notice ?

1. QU'EST-CE QUE SILOTRIF , gélule ET DANS QUELS CAS EST-IL UTILISE ?

Qu'est-ce que SILOTRIF ?
SILOTRIF appartient à un groupe de médicaments appelés inhibiteurs des récepteurs adrénergiques alpha-1A.

SILOTRIF agit de façon sélective sur les récepteurs situés dans la prostate, la vessie et l'urètre. En bloquant ces récepteurs, il provoque un relâchement du muscle lisse de ces tissus. Ceci vous permet d'uriner plus facilement et soulage vos symptômes.

Dans quel cas SILOTRIF est-il utilisé
SILOTRIF est utilisé chez l'homme adulte pour traiter les symptômes urinaires associés à l'hypertrophie bénigne de la prostate (augmentation du volume de la prostate), à l'exception des formes sévères, tels que :

- difficultés à commencer à uriner,
- sensation que la vessie n'est pas complètement vidée,
- besoin d'uriner plus fréquent, y compris la nuit.

2. QUELLES SONT LES INFORMATIONS A CONNAITRE AVANT DE PRENDRE SILOTRIF, gélule?

Ne prenez jamais SILOTRIF, gélule:
-si vous êtes allergique à la silodosine ou à l'un des autres composants contenus dans ce médicament, mentionnés dans la rubrique 6.

Avertissements et précautions
Adressez-vous à votre médecin, pharmacien ou votre infirmier/ère avant de prendre SILOTRIF.

- Si vous devez être opéré des yeux en raison d'une opacité du cristallin (opération de la cataracte), il est important que vous préveniez immédiatement votre ophtalmologiste que vous prenez ou avez pris SILOTRIF, car certains patients traités par ce type de médicament ont présenté une baisse du tonus musculaire de l'iris (la région circulaire colorée de l'œil) pendant ce type d'intervention. Votre ophtalmologiste pourra alors prendre les précautions appropriées quant aux techniques médicales et chirurgicales à utiliser. Demandez à votre médecin si vous devez ou non reporter ou interrompre temporairement votre traitement par SILOTRIF en cas d'opération de la cataracte.
- S'il vous est déjà arrivé de vous évanouir ou de ressentir des vertiges en vous levant rapidement, veuillez en informer votre médecin avant de prendre SILOTRIF.

La prise de SILOTRIF peut provoquer **des sensations vertigineuses** et occasionnellement des **évanouissements** lorsque vous vous relevez, en particulier en début de traitement ou si vous prenez d'autres médicaments faisant baisser la pression artérielle. Si ces effets se produisent, veillez à vous asseoir ou vous allonger immédiatement jusqu'à ce que les symptômes disparaissent et informez-en votre médecin dès que possible (voir également la rubrique « Conduite de véhicules et utilisation de machines »).

- Si vous avez de **sévères problèmes au foie**, vous ne devez pas prendre SILOTRIF car il n'a pas été testé dans cette maladie.
- Si vous avez des problèmes de reins, veuillez demander conseil auprès de votre médecin.

Si vos problèmes de reins sont modérés, votre médecin vous prescrira SILOTRIF avec prudence et éventuellement à une posologie réduite (voir la rubrique 3 « Posologie »).

Si vos problèmes de reins sont sévères, vous ne devez pas prendre SILOTRIF.

- L'hypertrophie bénigne de la prostate et le cancer de la prostate pouvant s'accompagner de symptômes identiques, votre médecin contrôlera que vous n'avez pas de cancer de la prostate avant d'entamer le traitement par SILOTRIF. SILOTRIF ne permet pas de traiter le cancer de la prostate.
- Le traitement par SILOTRIF peut entraîner des troubles de l'éjaculation (diminution de la quantité de sperme émise lors des rapports sexuels), ce qui peut affecter temporairement la fertilité masculine. Cet effet disparaît à l'arrêt du traitement par SILOTRIF. Veuillez prévenir votre médecin si vous projetez d'avoir un enfant.

Enfants et adolescents
Ne donnez pas ce médicament à des enfants ou des adolescents âgés de moins de 18 ans car il n'est pas indiqué dans cette tranche d'âge.

Autres médicaments et SILOTRIF, gélule
Informez votre médecin ou pharmacien si vous prenez, avez récemment pris ou pourriez prendre tout autre médicament.

En particulier, prévenez votre médecin si vous prenez :

- **des médicaments permettant de baisser la pression artérielle** (en particulier les médicaments appelés inhibiteurs des récepteurs alpha1, comme la prazosine ou la doxazosine) car la prise concomitante de SILOTRIF peut entraîner une augmentation des effets de ces médicaments ;
- **des médicaments antifongiques** (comme le kétoconazole ou l'itraconazole), des médicaments contre l'infection par le VIH/SIDA (comme le ritonavir) ou des médicaments utilisés après des greffes d'organe pour prévenir le rejet (comme la ciclosporine) car ces médicaments peuvent augmenter la concentration de SILOTRIF dans le sang ;
- **des médicaments utilisés pour traiter les problèmes d'érection** (comme le sildénafil ou le tadalafil) car leur utilisation en même temps que SILOTRIF peut entraîner une légère baisse de la pression artérielle ;
- **des médicaments contre l'épilepsie ou de la rifampicine** (médicament utilisé pour traiter la tuberculose) car ceux-ci peuvent réduire les effets de SILOTRIF.

Grossesse et allaitement
SILOTRIF n'est pas destiné aux femmes.

Fertilité
SILOTRIF peut réduire la quantité de sperme, ce qui peut temporairement affecter votre capacité à concevoir un enfant. Si vous prévoyez d'avoir un enfant, demandez conseil à votre médecin ou votre pharmacien avant de prendre ce médicament.

Conduite de véhicules et utilisation de machines
Il est déconseillé de conduire ou d'utiliser des machines si vous sentez que vous risquez de vous évanouir ou de vous endormir, si vous êtes pris de vertiges ou si votre vision est trouble.

3. COMMENT PRENDRE SILOTRIF, gélule?

Veillez à toujours prendre ce médicament en suivant exactement les indications de votre médecin ou pharmacien. Vérifiez auprès de votre médecin ou pharmacien en cas de doute.
La dose recommandée est d'une gélule de SILOTRIF 8 mg par jour, par voie orale.

Prenez toujours votre gélule pendant un repas, de préférence à heure fixe. N'ouvrez pas et ne croquez pas la gélule mais avalez-la entière, de préférence avec un verre d'eau.

Patients ayant des problèmes de reins
Si vous avez des problèmes de reins modérés, votre médecin pourra vous prescrire une posologie différente. C'est pourquoi des gélules de SILOTRIF 4 mg sont disponibles.

Si vous avez pris plus de SILOTRIF, gélule que vous n'auriez dû
Si vous avez pris plus d'une gélule, informez-en votre médecin dès que possible. Si vous avez des vertiges ou si vous vous sentez faible, prévenez votre médecin immédiatement.

Si vous oubliez de prendre SILOTRIF, gélule
Si vous avez oublié de prendre votre gélule à l'heure prévue, vous pouvez la prendre plus tard dans la journée. S'il est presque l'heure de prendre la dose suivante, ne prenez pas la dose oubliée. Ne prenez pas de dose double pour compenser la gélule que vous avez oubliée de prendre.

Si vous arrêtez de prendre SILOTRIF, gélule
Si vous arrêtez le traitement, vos symptômes peuvent réapparaître.

Si vous avez d'autres questions sur l'utilisation de ce médicament, demandez plus d'informations à votre médecin ou à votre pharmacien.

4. QUELS SONT LES EFFETS INDESIRABLES EVENTUELS ?

Comme tous les médicaments, ce médicament peut provoquer des effets indésirables, mais ils ne surviennent pas systématiquement chez tout le monde.
Contactez immédiatement votre médecin si vous remarquez l'une des réactions allergiques suivantes : gonflement du visage ou de la gorge, difficultés à respirer, sensation d'évanouissement, démangeaisons ou urticaire, car ceci pourrait avoir de graves conséquences.

L'effet indésirable le plus fréquent est une diminution de la quantité de sperme émise pendant les rapports sexuels. Cet effet disparaît à l'arrêt du traitement par SILOTRIF Veuillez prévenir votre médecin si vous projetez d'avoir un enfant.

Des sensations vertigineuses, survenant notamment lorsque vous vous levez, et occasionnellement des évanouissements, peuvent se produire.

Si vous vous sentez faible ou si vous avez des vertiges, veillez à vous asseoir ou vous allonger immédiatement jusqu'à ce que les symptômes disparaissent. Si vous avez des vertiges en vous mettant debout ou si vous vous évanouissez, veuillez en informer votre médecin dès que possible.

SILOTRIF peut provoquer des complications lors d'une opération de la cataracte (opération des yeux en raison d'une opacité du cristallin ; voir rubrique « Mises en Garde et précautions »).

Il est important que vous préveniez immédiatement votre ophtalmologiste si vous prenez ou avez pris SILOTRIF

Les effets indésirables potentiels sont présentés ci-dessous :

Effets indésirables très fréquents (peuvent affecter plus d'un patient sur 10)

· Troubles de l'éjaculation (émission réduite ou nulle de sperme lors des rapports sexuels ; voir la rubrique « Mises en Garde et précautions »)

Effets indésirables fréquents (peuvent affecter jusqu'à 1 patient sur 10)

· Sensations vertigineuses, notamment lors du passage à la position debout (voir également ci-dessus dans cette rubrique)

· Nez qui coule ou nez bouché

· Diarrhée

Effets indésirables peu fréquents (peuvent affecter jusqu'à 1 patient sur 100)

· Diminution du désir sexuel

· Nausées

· Bouche sèche

· Difficultés à obtenir ou maintenir une érection

· Rythme cardiaque accéléré

· Symptômes de réaction allergique touchant la peau, tels que rash, démangeaisons, urticaire et éruption provoquée par un médicament

· Résultats anormaux des tests de la fonction hépatique

· Pression artérielle basse

Effets indésirables rares (peuvent affecter jusqu'à 1 patient sur 1000)

· Rythme cardiaque rapide ou irrégulier (palpitations)

· Évanouissement/perte de conscience

Effets indésirables très rares (peuvent affecter jusqu'à 1 patient sur 10 000)

· Autres réactions allergiques avec gonflement du visage ou de la gorge

Fréquence indéterminée (ne peut être estimée sur la base des données disponibles)

· Iris hypotonique lors d'une opération de la cataracte (voir également ci-dessus dans cette rubrique).

Si vous pensez que votre vie sexuelle est affectée, parlez-en à votre médecin.

Déclaration des effets secondaires
Si vous ressentez un quelconque effet indésirable, parlez-en à votre médecin, votre pharmacien. Ceci s'applique aussi à tout effet indésirable qui ne serait pas mentionné dans cette notice. Vous pouvez également déclarer les effets indésirables directement via le système national de déclaration : Agence Nationale du médicament

En signalant les effets indésirables, vous contribuez à fournir davantage d'informations sur la sécurité du médicament.

5. COMMENT CONSERVER SILOTRIF, gélule?

A conserver à une température ne dépassant pas 30°C à l'abri de la lumière et de l'humidité.

Tenir hors de la vue et de la portée des enfants.

N'utilisez pas ce médicament après la date de péremption indiquée sur l'étui et la plaquette. La date de péremption fait référence au dernier jour de ce mois.

Ne jetez aucun médicament au tout-à-l'égout ou avec les ordures ménagères. Demandez à votre pharmacien d'éliminer les médicaments que vous n'utilisez plus. Ces mesures contribueront à protéger l'environnement.

6. CONTENU DE L'EMBALLAGE ET AUTRES INFORMATIONS

Ce que contient SILOTRIF,gélules

- **SILOTRIF 4 mg gélules**
- substance active :

Silodosine.....4 mg

Pour une gélule.

- Les autres composants sont :

Contenu de la gélule
Mannitol (E421), Amidon prégélatinisé, Laurylsulfate de sodium, Stéarate de magnésium.

Enveloppe de la gélule
Gélatine, Méthylparabène, Propylparabène, Laurylsulfate de sodium, Eau purifiée, Colorant bleu brillant, Carmoisine (E122), Tartrazine (E102), Dioxyde de titane (E171).

- **SILOTRIF 8 mg gélules**
- substance active :

Silodosine.....8 mg

Pour une gélule.

- Les autres composants sont :

Contenu de la gélule

Mannitol (E421), Amidon prégélatinisé, Laurylsulfate de sodium, Stéarate de magnésium.

Enveloppe de la gélule

Gélatine, Méthylparabène, Propylparabène, Laurylsulfate de sodium, Eau purifiée, Colorant jaune soleil, Tartrazine (E102), Dioxyde de titane (E171).

Qu'est-ce que SILOTRIF , gélule et contenu de l'emballage extérieur
- Boîte de 30 gélules : 3 blister de 10 gélules.
Blister (Aluminium/Aluminium).

Titulaire de l'autorisation de mise sur le marché
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La dernière date à laquelle cette notice a été révisée est :
MAI 2022

B32958-00

1.3.3 Package Insert (also known as patient information PIL)

Patient Information leaflet for SILOTRIF 4 (Silodosin Capsules 4 mg)

has been enclosed inthe following pages.

Package Leaflet: Information for the patient

Silodisin capsules 4 mg and 8 mg

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

-Keep this leaflet. You may need to read it again.

-If you have any further questions, ask your doctor or pharmacist.

-This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.

-If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1.What Silodisin is and what it is used for

What Silodisin is

Silodisin belongs to a group of medicines called alpha JA-adrenoreceptor blockers.

Silodisin is selective for the receptors located in the prostate, bladder and urethra. By blocking these receptors, it causes smooth muscle in these tissues to relax. This makes it easier for you to pass water and relieves your symptoms.

2.What Silodisin is used for

Silodisin is used in adult men to treat the urinary symptoms associated with benign enlargement of the prostate (prostatic hyperplasia), such as:

- difficulty in starting to pass water,
- a feeling of not completely emptying the bladder,
- a more frequent need to pass water, even at night.

3.What you need to know before you take Silodisin Capsules

Do not take Silodisin Capsules

if you are allergic to silodosin or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

Talk to your doctor or pharmacist before taking Silodisin Capsules

•If you are undergoing eye surgery because of cloudiness of the lens (cataract surgery), it is important that you immediately inform your eye specialist that you are using or have previously used Silodisin . This is because some patients treated with this kind of medicine experienced a loss of muscle tone in the iris (the coloured circular part of the eye) during such a surgery. The specialist can take appropriate precautions with respect to medicine and surgical techniques to be used. Ask your doctor whether or not you should postpone or temporarily stop taking Silodisin Capsules when undergoing cataract surgery.

•If you have ever fainted or felt dizzy when suddenly standing up, please inform your doctor before taking Silodisin Capsules.

•Dizziness when standing up and occasionally fainting may occur when taking Silodisin Capsules, particularly when starting treatment or if you are taking other medicines that lower blood pressure. If this occurs, make sure you sit or lie down straight away until the symptoms have disappeared and inform your doctor as soon as possible (see also section "Driving and using machines").

•If you have severe liver problems, you should not take Silodisin Capsules, as it was not tested in this condition.

•If you have problems with your kidneys, please ask your doctor for advice.

If you have moderate kidney problems, your doctor will start Silodisin Capsules with caution and possibly with a lower dose (see section 3 "Dose").

If you have severe kidney problems, you should not take Silodisin Capsules.

•Since a benign enlargement of the prostate and prostate cancer may present the same symptoms, your doctor will check you for prostate cancer before starting treatment with Silodisin Capsules. Silodisin Capsules does not treat prostate cancer.

•The treatment with Silodisin may lead to an abnormal ejaculation (decrease in the amount of semen released during sex) that may temporarily affect male fertility. This effect disappears after discontinuation of Silodisin . Please inform your doctor if you are planning to have children.

Children and adolescents

Do not give this medicine to children and adolescents below 18 years since there is no relevant indication for this age group.

Other medicines and Silodisin Capsules

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Tell your doctor in particular, if you take:

•**medicines which lower blood pressure** (in particular, medicines called alphai-blockers, such as prazosin or doxazosin) as there may be the potential risk that the effect of these medicines is increased whilst taking Silodisin .

•**antifungal medicines** (such as ketoconazole or itraconazole), **medicines used for HIV-AIDS (such as ritonavir) or medicines used after transplants to prevent organ rejection** (such as cyclosporin) because these medicines can increase the blood concentration of Silodisin .

•**medicines used for treating problems in getting or keeping an erection** (such as sildenafil or tadalafil), since the concomitant use with Silodisin might lead to a slight decrease in blood pressure.

•**medicines for epilepsy or rifampicin** (a medicine to treat tubercolosis), since the effect of Silodisin may be reduced.

Driving and using machines

Do not drive or operate machines if you feel faint, dizzy, drowsy or have blurred vision.

3. How to take Silodisin Capsules

Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

The recommended dose is one capsule of Silodisin 8 mg per day by oral administration.

Take the capsule always with food, preferably at the same time every day. Do not break or chew the capsule, but swallow it whole, preferably with a glass of water.

Patients with kidney problems

If you have moderate kidney problems, your doctor may prescribe a different dose. For this purpose Silodisin 4 mg hard capsules are available.

If you take more Silodisin Capsules than you should

If you have taken more than one capsule, inform your doctor as soon as possible. If you become dizzy or feel weak, tell your doctor straight away.

If you forget to take Silodisin Capsules

You may take your capsule later the same day if you have forgotten to take it earlier. If it is almost time for the next dose, skip the dose you missed. Do not take a double dose to make up for a forgotten capsule.

If you stop taking Silodisin

If you stop treatment, your symptoms may re-appear.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4.Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Contact your doctor immediately if you notice any of the following allergic reactions: swelling of the face or throat, difficulty in breathing, feeling faint, itchy skin or hives since the consequences could become serious.

The most common side effect is a decrease in the amount of semen released during sex. This effect disappears after discontinuation of Silodisin . Please inform your doctor if you are planning to have children.

Dizziness, including dizziness when standing up, and occasionally fainting, may occur.

If you do feel weak or dizzy, make sure you sit or lie down straight away until the symptoms have disappeared. If dizziness when standing up or fainting occurs, please inform your doctor as soon as possible.

Silodisin may cause complications during a cataract surgery (eye surgery because of cloudiness of the lens, see section "Warnings and precautions").

It is important that you immediately inform your eye specialist if you are using or have previously used Silodisin .

The possible side effects are listed below:

Very common side effects (may affect more than 1 in 10 people)

•Abnormal ejaculation (less or no noticeable semen is released during sex, see section "Warnings and precautions")

Common side effects (may affect up to 1 in 10 people)

•Dizziness, including dizziness when standing up (see also above, in this section)

•Runny or blocked nose

•Diarrhoea

Uncommon side effects (may affect up to 1 in 100 people)

•Decreased sexual drive

•Nausea

•Dry mouth

•Difficulties in getting or keeping an erection

•Faster heart rate

•Symptoms of allergic reaction affecting the skin like rash, itching, hives and rash caused by a medicine

•Abnormal results of liver function tests

•Low blood pressure

Rare side effects (may affect up to 1 in 1,000 people)

•Fast or irregular heart beats (called palpitations)

•Fainting/ Loss of consciousness

Very rare side effects (may affect up to 1 in 10,000people)

•Other allergic reactions with swelling of the face or throat

Not known (frequency cannot be estimated from the available data)

•Floppy pupil during cataract surgery (see also above, in this section)

If you feel that your sexual life is affected, please tell your doctor.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

By reporting side effects you can help provide more information on the safety of this medicine.

5.How to store Silodisin Capsules

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 strip 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.

Do not use this medicine if you notice that is damaged or shows signs of tampering.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Silodisin Capsules contains

Capsule contents

Mannitol , Pregelatinised starch ,Sodium lauryl sulphate , Magnesium Stearate

Capsule shell contents

Capsule shell contents

4 mg: size “3” hard gelatin capsules with grey color body and red color cap.

Composition: Gelatin, Methylparaben, Propylparaben, Sodium Lauryl Sulphate, Purified Water, Brilliant Blue, Carmoisine, Tartrazine, Titanium dioxide.

8 mg: size “2” hard gelatin capsules with golden yellow color body and golden yellow color cap.

Composition: Gelatin ,Methyl Paraben, Propyl Paraben, Sodium Lauryl Sulfate, Purified Water, Sunset yellow, Tartrazine, Titanium Dioxide.

What Silodisin Capsules looks like and contents of the pack

Silodisin Capsules 4 mg: White to off white color granular powder was filled in size "3" hard gelatin capsules with grey color body and red color cap..

Silodisin Capsules 8 mg: White to off white color granular powder was filled in size "2" hard gelatin capsules with golden yellow color body and golden yellow color cap.

Silodisin Capsules are available in 10's Alu – Alus strip pack

Marketing Authorisation Holder

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