ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Urorec 4 mg hard capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each hard capsule contains 4 mg silodosin.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Hard capsule.

Yellow, opaque, hard gelatin capsule, size 3.

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 Urorec 8 mg daily. For special patient populations, one capsule of Urorec 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 Urorec 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

Urorec 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			

	Very common	*Common*	*Uncommon*	*Rare*	*Very rare*	*Not known*
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).

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

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 Urorec 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 Urorec 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 content
Starch, pregelatinised (maize)
Mannitol (E421)
Magnesium stearate
Sodium laurilsulfate

Capsule shell
Gelatin
Titanium dioxide (E171)
Yellow iron oxide (E172)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 30°C.
Store in the original package in order to protect from light and moisture.

6.5 Nature and contents of container

The capsules are provided in PVC/PVDC/aluminium foil blisters, packed in cartons.

Packs of 5, 10, 20, 30, 50, 90, 100 capsules.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Recordati Ireland Ltd.
Raheens East
Ringaskiddy Co. Cork
Ireland

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/09/608/001
EU/1/09/608/002
EU/1/09/608/003
EU/1/09/608/004
EU/1/09/608/005
EU/1/09/608/006
EU/1/09/608/007

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 29/01/2010
Date of latest renewal: 18/09/2014

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

1. NAME OF THE MEDICINAL PRODUCT

Urorec 8 mg hard capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each hard capsule contains 8 mg silodosin.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Hard capsule.

White, opaque, hard gelatin capsule, size 0.

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

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

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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 Urorec 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.

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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.

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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.

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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.

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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.

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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			

	Very common	*Common*	*Uncommon*	*Rare*	*Very rare*	*Not known*
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).

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

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 Urorec 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 Urorec 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 content
Starch, pregelatinised (maize)
Mannitol (E421)
Magnesium stearate
Sodium laurilsulfate

Capsule shell
Gelatin
Titanium dioxide (E171)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 30°C.

Store in the original package in order to protect from light and moisture.

6.5 Nature and contents of container

The capsules are provided in PVC/PVDC/aluminium foil blisters, packed in cartons.

Packs of 5, 10, 20, 30, 50, 90, 100 capsules.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Recordati Ireland Ltd.
Raheens East
Ringaskiddy Co. Cork
Ireland

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/09/608/008
EU/1/09/608/009
EU/1/09/608/010
EU/1/09/608/011
EU/1/09/608/012
EU/1/09/608/013
EU/1/09/608/014

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 29/01/2010
Date of latest renewal: 18/09/2014

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer(s) responsible for batch release

Recordati Industria Chimica e Farmaceutica S.p.A.
Via M. Civitali 1
20148 Milan
Italy

LABORATOIRES BOUCHARA-RECORDATI
Parc Mécatronic
03410 Saint Victor
France

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic Safety Update Reports**

The marketing authorisation holder shall submit periodic safety update reports for this product in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk Management Plan (RMP)**

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

If the dates for submission of a PSUR and the update of a RMP coincide, they can be submitted at the same time.

- **Additional risk minimisation measures**

The MAH shall ensure that all eye surgeons in the EU Countries in which silodosin will be marketed are provided with the following information:

- the Direct Healthcare Professional Communication (DHPC) on the association of Silodosin with Intraoperative Floppy Iris Syndrome and the two literature references mentioned in the text of the communication (at launch);

- a flow-chart describing the management of patients for which cataract surgery is scheduled (at launch and after launch);
- an educational program on the prevention and management of IFIS (at launch and after launch); covering the following topics:

    1. clinically relevant literature references on the prevention and management of IFIS;
    2. pre-operative assessment: eye surgeons and ophthalmic teams should establish whether patients scheduled for cataract surgery are being or have been treated with silodosin in order to ensure that appropriate measures are in place to manage IFIS during surgery.
    3. recommendation to surgeons and ophthalmic teams: discontinuing treatment with α1-adrenoceptor antagonists 2 weeks prior to cataract surgery has been recommended, but the benefit and duration of stopping therapy prior to cataract surgery has not yet been established.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Urorec 4 mg hard capsules

silodosin

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each hard capsule contains 4 mg silodosin.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

5 hard capsules
10 hard capsules
20 hard capsules
30 hard capsules
50 hard capsules
90 hard capsules
100 hard capsules

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

Oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Do not store above 30°C.
Store in the original package in order to protect from light and moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Recordati Ireland Ltd.
Raheens East
Ringaskiddy Co. Cork
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/09/608/001
EU/1/09/608/002
EU/1/09/608/003
EU/1/09/608/004
EU/1/09/608/005
EU/1/09/608/006
EU/1/09/608/007

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Urorec 4 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC:
SN:
NN:

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

PVC/PVDC/aluminium foil blisters

1. NAME OF THE MEDICINAL PRODUCT

Urorec 4 mg hard capsules

silodosin

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Recordati Ireland Ltd.

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Urorec 8 mg hard capsules

silodosin

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each hard capsule contains 8 mg silodosin.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

5 hard capsules
10 hard capsules
20 hard capsules
30 hard capsules
50 hard capsules
90 hard capsules
100 hard capsules

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

Oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Do not store above 30°C.
Store in the original package in order to protect from light and moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Recordati Ireland Ltd.
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12. MARKETING AUTHORISATION NUMBER(S)

EU/1/09/608/008
EU/1/09/608/009
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EU/1/09/608/012
EU/1/09/608/013
EU/1/09/608/014

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Urorec 8 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC:

SN:
NN:

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

PVC/PVDC/aluminium foil blisters

1. NAME OF THE MEDICINAL PRODUCT

Urorec 8 mg hard capsules

silodosin

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Recordati Ireland Ltd.

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

B. PACKAGE LEAFLET

Package Leaflet: Information for the patient

Urorec 8 mg hard capsules
Urorec 4 mg hard capsules
Silodosin

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 Urorec is and what it is used for

What Urorec is

Urorec belongs to a group of medicines called alpha$_{1A}$-adrenoreceptor blockers.
Urorec 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.

What Urorec is used for

Urorec 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.

2. What you need to know before you take Urorec

Do not take Urorec

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 Urorec

- 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 Urorec. 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 Urorec when undergoing cataract surgery.

- If you have ever fainted or felt dizzy when suddenly standing up, please inform your doctor before taking Urorec.
  Dizziness when standing up and occasionally **fainting** may occur when taking Urorec, 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 Urorec, 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 Urorec with caution and possibly with a lower dose (see section 3 "Dose").
  If you have severe kidney problems, you should not take Urorec.

- 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 Urorec. Urorec does not treat prostate cancer.

- The treatment with Urorec 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 Urorec. 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 Urorec

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 alpha$_1$-blockers, such as prazosin or doxazosin) as there may be the potential risk that the effect of these medicines is increased whilst taking Urorec.
- **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 Urorec.
- **medicines used for treating problems in getting or keeping an erection** (such as sildenafil or tadalafil), since the concomitant use with Urorec might lead to a slight decrease in blood pressure.
- **medicines for epilepsy or rifampicin** (a medicine to treat tubercolosis), since the effect of Urorec 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 Urorec

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 Urorec 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 Urorec 4 mg hard capsules are available.

If you take more Urorec 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 Urorec

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 Urorec

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 Urorec. 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.

Urorec 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 Urorec.

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 10,000 people)
- 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. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Urorec

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 blister after EXP. The expiry date refers to the last day of that month.

Do not store above 30°C.
Store in the original package in order to protect from light and moisture.

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 Urorec contains

Urorec 8 mg
The active substance is silodosin. Each capsule contains 8 mg of silodosin.

The other ingredients are pregelatinised maize starch, mannitol (E421), magnesium stearate, sodium laurilsulfate, gelatin, titanium dioxide (E171).

Urorec 4 mg
The active substance is silodosin. Each capsule contains 4 mg of silodosin.

The other ingredients are pregelatinised maize starch, mannitol (E421), magnesium stearate, sodium laurilsulfate, gelatin, titanium dioxide (E171), yellow iron oxide (E172).

What Urorec looks like and contents of the pack

Urorec 8 mg are white, opaque, hard gelatin capsules.

Urorec 4 mg are yellow, opaque, hard gelatin capsules.

Urorec is available in packs containing 5, 10, 20, 30, 50, 90, 100 capsules. Not all pack sizes may be marketed.

Marketing Authorisation Holder

Recordati Ireland Ltd.
Raheens East
Ringaskiddy Co. Cork
Ireland

Manufacturer

Recordati Industria Chimica e Farmaceutica S.p.A.
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Other sources of information
Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.