Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Kirnom XL 400 micrograms Prolonged-Release Hard Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains tamsulosin hydrochloride 400 microgram, equivalent to 367 microgram tamsulosin.

For full list of the excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Prolonged-release capsule, hard
Kirnom XL Capsules consist of a light green opaque cap and light yellowopaque body containing white to off white pellets, imprinted with $\overset{W}{516}$ on the cap with black ink.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Lower urinary tract symptoms (LUTS)associated with benign prostatic hyperplasia (BPH).

4.2 Posology and method of administration

For oral use
One Capsule daily, to be taken after the same meal each day.
The capsule should be swallowed whole and should not be crunched or chewed as this will interfere with the modified release of the active ingredient.

Paediatric Population
The safety and efficacy of tamsulosin in children <18 years have not been established. Currently available data are described in section 5.1.

4.3 Contraindications

Hypersensitivity to tamsulosin hydrochloride or to any other component of the product (see section 6.1); a history of orthostatic hypotension; severe hepatic insufficiency.

4.4 Special warnings and precautions for use

As with other alpha$_1$ blockers, a reduction in blood pressure can occur in individual cases during treatment with Kirnom XL, as a result of which, rarely, syncope can occur. At the first signs of orthostatic hypotension (dizziness, weakness) the patient should sit or lie down until the symptoms have disappeared.

Before therapy with Kirnom XL is initiated the patient should be examined in order to exclude the presence of other conditions which can cause the same symptoms as benign prostatic hyperplasia. Digital rectal examination and when necessary determination of prostate specific antigen (PSA) should be performed before treatment and at regular intervals afterwards.

The treatment of severely renally impaired patients (creatinine clearance of less than 10 ml/min) should be approached with caution as these patients have not been studied.

The 'Intraoperative Floppy Iris Syndrome' (IFIS, a variant of small pupil syndrome) has been observed during cataract surgery in some patients on or previously treated with tamsulosin hydrochloride. IFIS may lead to increased procedural complications during the operation.

Discontinuing tamsulosin hydrochloride 1 – 2 weeks prior to cataract surgery is anecdotally considered helpful, but the benefit and duration of stopping of therapy prior to cataract surgery has not yet been established. IFIS has also been reported in patients who had discontinued tamsulosin for a longer period prior to the surgery.

The initiation of therapy with tamsulosin hydrochloride in patients for whom cataract surgery is scheduled is not recommended. During pre-operative assessment, cataract surgeons and ophthalmic teams should consider whether patients scheduled for cataract surgery are being or have been treated with tamsulosin in order to ensure that appropriate measures will be in place to manage the IFIS during surgery.

Tamsulosin hydrochloride should not be given in combination with strong inhibitors of CYP3A4 (e.g. ketoconazole) in patients with poor metaboliser CYP2D6 phenotype.

Tamsulosin hydrochloride should be used with caution in combination with strong (e.g. ketoconazole) and moderate (e.g. erythromycin) inhibitors of CYP3A4 (see section 4.5).

4.5 Interaction with other medicinal products and other forms of interactions

Interaction studies have only been performed in adults.

No interactions have been seen when Kirnom XL was given concomitantly with either atenolol, enalapril , nifedipine or theophylline. Concomitant cimetidine brings about a rise in plasma levels of tamsulosin, and furosemide a fall, but as levels remain within the normal range posology need not be changed.

In vitro, neither diazepam, nor propranolol, trichlormethiazide, chlormadinon, amitriptyline, diclofenac, glibenclamide, simvastatin, and warfarin change the free fraction of tamsulosin in human plasma. Neither does tamsulosin change the free fractions of diazepam, propranolol, trichlormethiazide, and chlormadinone.

Diclofenac and warfarin, however, may increase the elimination rate of tamsulosin.

Concomitant administration of tamsulosin hydrochloride with strong inhibitors of CYP3A4 may lead to increased exposure to tamsulosin hydrochloride. Concomitant administration with ketoconazole (a known strong CYP3A4 inhibitor) resulted in an increase in AUC and Cmax of tamsulosin hydrochloride by a factor of 2.8 and 2.2, respectively.

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Concomitant administration of tamsulosin hydrochloride with paroxetine, a strong inhibitor of CYP2D6, resulted in a Cmax and AUC of tamsulosin that had increased by a factor of 1.3 and 1.6, respectively, but these increases are not considered clinically relevant.

There is a theoretical risk of enhanced hypotensive effect when given concurrently with drugs which may reduce blood pressure, including anaesthetic agents and other α_1-adrenoceptor antagonists.

4.6 Fertility, pregnancy and lactation

Kirnom XL is not indicated for use in women.

Ejaculation disorders have been observed in short and long term clinical studies with tamsulosin. Events of ejaculation disorder, retrograde ejaculation and ejaculation failure have been reported in the post authorisation phase.

4.7 Effects on ability to drive and use machines

No data is available on whether Kirnom XL adversely affects the ability to drive or operate machines. However, in this respect patients should be aware of the fact that drowsiness, blurred vision, dizziness and syncope can occur.

4.8 Undesirable effects

System Organ Class	Common (>1/100, <1/10)	Uncommon (>1/1000, <1/100)	Rare (>1/10,000, <1/1000)	Very rare (<1/10,000)	Unknown (cannot be estimated from the available data)
Nervous system disorders	Dizziness (1.3%)	Headache	Syncope		
Eye disorders					Vision blurred*, vision impaired*
Cardiac disorders		Palpitations			
Vascular disorders		Orthostatic hypotension			
Respiratory, thoracic and mediastinum-related disorders		Rhinitis			Epistaxis*
Gastrointestinal disorders		Constipation, diarrhoea, nausea, vomiting			Dry mouth*
Skin and subcutaneous tissue disorders		Rash, pruritus, urticaria	Angioedema	Stevens-Johnson syndrome	Erythema multiforme*, dermatitis exfoliative*
Reproductive systems and breast disorders	Ejaculation disorders, including retrograde ejaculation, ejaculation failure			Priapism	
General disorders and administration site conditions		Asthenia			

*observed post-marketing.
As with other alpha-blockers, drowsiness, blurred vision or oedemia can occur.
During cataract surgery a small pupil situation, known as Intraoperative Floppy Iris Syndrome (IFIS), has been associated with therapy of tamsulosin during post-marketing surveillance (see also section 4.4)
Post-marketing experience: In addition to the adverse events listed above, atrial fibrillation, arrhythmia, tachycardia and dyspnoea have been reported in association with tamsulosin use. Because these spontaneously reported events are from the worldwide post-marketing experience, the frequency of events and the role of tamsulosin in their causation cannot be estimated from the available data.

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; e-mail: medsafety@hpra.ie

4.9 Overdose

Symptoms:

Overdosage with tamsulosin hydrochloride can potentially result in severe hypotensive effects, dizziness and malaise. Severe hypotensive effects have been observed at different levels of overdosing.

Treatment:

In case of acute hypotension occurring after overdosage cardiovascular support should be given. Blood pressure can be restored and heart rate brought back to normal by lying the patient down. If this does not help then volume expanders, and when necessary, vasopressors could be employed. Renal function should be monitored and general supportive measures applied. Dialysis is unlikely to be of help as tamsulosin is very highly bound to plasma proteins.

Measures, such as emesis, can be taken to impede absorption. When large quantities are involved, gastric lavage can be applied and activated charcoal and an osmotic laxative, such as sodium sulphate, can be administered

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group:

ATC Code G04C A02
Alpha1-adrenoceptor antagonist.

Preparations for the exclusive treatment of prostatic disease.

Mechanism of action:

Tamsulosin binds selectively and competitively to postsynaptic alpha1-receptors, in particular to the subtype alpha1A, which bring about relaxation of the smooth muscle of the prostate, whereby tension is reduced.

Pharmacodynamic effects:

Kirnom XL increases maximum urinary flow rate by reducing smooth muscle tension in prostate and urethra and thereby relieving obstruction.

It also improves the complex of irritative and obstructive symptoms in which bladder instability and tension of the smooth muscles of the lower urinary tract play an important role.

Alpha1-blockers can reduce blood pressure by lowering peripheral resistance. No reduction in blood pressure of any clinical significance was observed during studies with Kirnom XL.

Paediatric Population
A double-blind, randomized, placebo-controlled, dose ranging study was performed in children with neuropathic bladder. A total of 161 children (with an age of 2 to 16 years) were randomized and treated at 1 of 3 dose levels of tamsulosin (low [0.001 to 0.002 mg/kg], medium [0.002 to 0.004 mg/kg], and high [0.004 to 0.008 mg/kg]), or placebo. The primary endpoint was number of patients who decreased their detrusor leak point pressure (LPP) to <40 cm H_2O based upon two evaluations on the same day. Secondary endpoints were: Actual and percent change from baseline in detrusor leak point pressure, improvement or stabilization of hydronephrosis and hydroureter and change in urine volumes obtained by catheterisation and number of times wet at time of catheterisation as recorded in catheterisation diaries. No statistically significant difference was found between the placebo group and any of the 3 tamsulosin dose groups for either the primary or any secondary endpoints. No dose response was observed for any dose level.

5.2 Pharmacokinetic properties

Absorption:

Tamsulosin is absorbed from the intestine and is almost completely bioavailable.

Absorption of tamsulosin is reduced by a recent meal.

Uniformity of absorption can be promoted by the patient always taking Kirnom XL after the same meal each day.

Tamsulosin shows linear kinetics. After a single dose of Kirnom XL in the fed state, plasma levels of tamsulosin peak at around 6 hours and, in the steady state, which is reached by day 5 of multiple dosing, C_{max} in patients is about two thirds higher than that reached after a single dose. Although this was seen in elderly patients, the same finding would also be expected in young ones.

There is a considerable inter-patient variation in plasma levels both after single and multiple dosing.

Distribution:

In man, tamsulosin is about 99% bound to plasma proteins and volume of distribution is small (about 0.2 l/kg).

Biotransformation:

Tamsulosin has a low first pass effect, being metabolised slowly. Most tamsulosin is present in plasma in the form of unchanged drug. It is metabolised in the liver.

In rats, hardly any induction of microsomal liver enzymes was seen to be caused by tamsulosin.

In vitro results suggest that CYP3A4 and also CYP2D6 are involved in metabolism, with possible minor contributions to tamsulosin hydrochloride metabolism by other CYP isozymes. Inhibition of CYP3A4 and CYP2D6 drug metabolizing enzymes may lead to increased exposure to tamsulosin
hydrochloride (see section 4.4 and 4.5).

No dose adjustment is warranted in hepatic insufficiency.

None of the metabolites are more active than the original compound.

Elimination:

Tamsulosin and its metabolites are mainly excreted in the urine with about 9% of a dose being present in the form of unchanged drug.

After a single dose of Kirnom XL in the fed state, and in the steady state in patients, elimination half-lives of about 10 and 13 hours respectively have been measured.

The presence of renal impairment does not warrant lowering the dose.

5.3 Preclinical safety data

Single and repeat dose toxicity studies were performed in mice, rats and dogs. In addition reproduction toxicity studies were performed in rats, carcinogenicity in mice and rats and in vivo and in vitro genotoxicity were examined. The general toxicity profile as seen with high doses of tamsulosin is consistent with the known pharmacological actions of the alpha-adrenergic blocking agents. At very high dose levels the ECG was altered in dogs. This response is considered to be not clinically relevant. Tamsulosin showed no relevant genotoxic properties.

Increased incidences of proliferative changes of mammary glands of female rats and mice have been reported. These findings which are probably mediated by hyperprolactinaemia and only occurred at high dose levels are regarded as irrelevant.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule contents:
Microcrystalline cellulose

Methacrylic acid–ethyl acrylate copolymer (1:1) dispersion 30 per cent
Talc
Purified water
Magnesium stearate
Triethyl citrate

Capsule shell contents:
Hard gelatin
Sodium laurilsulfate
Quinoline yellow E104
Titanium dioxide E171
Brilliant blue E133

Black imprinting ink (TekPrintTM SW-9008):
Shellac
Black iron oxide E172

6.2 Incompatibilities

None known.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Blister strips (PVC/PE/PVDC base, aluminium lid) containing 10 capsules contained in a cardboard box.
Pack sizes of 30 capsules.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special instructions.

Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Wockhardt UK Limited
Ash Road North
Wrexham
LL13 9UF
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA1339/020/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 24th September 2010

10 DATE OF REVISION OF THE TEXT

February 2017