Public Assessment Report

Decentralised Procedure

Faramsil 400 microgram Prolonged-release Tablets

Tamsulosin 400 microgram Prolonged-release Tablets

PL 04416/0987-0989

PL 04416/1220-1221

UK/H/2481-2483/001/DC

UK/H/4466-4467/001/DC

Sandoz Ltd
Lay summary

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Sandoz Ltd Marketing Authorisations (licences) for the medicinal products Faramsil 400 microgram Prolonged-release Tablets (product licence number: PL 04416/0987) and Tamsulosin 400 microgram Prolonged-release Tablets (PL 04416/0988-0989 and PL 04416/1220-1221) on 14 July 2011. These medicines are available on prescription only.

Faramsil 400 microgram Prolonged-release Tablets are identical to Tamsulosin 400 microgram Prolonged-release Tablets, apart from the difference in product name. These products contain the active ingredient tamsulosin hydrochloride, which belongs to a group of medicines called the alpha adrenoceptor blockers. Tamsulosin hydrochloride relaxes the muscles in the prostate gland and the tube from the bladder to the outside, making it easier to urinate.

The data submitted in support of these applications for Faramsil 400 microgram Prolonged-release Tablets and Tamsulosin 400 microgram Prolonged-release Tablets raised no clinically significant safety concerns and it was, therefore, judged that the benefits of using these products outweigh the risks; hence Marketing Authorisations have been granted.
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2 Quality aspects  
3 Preclinical aspects  
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### Module 1

#### Information about Decentralised Procedure

| Names of the products in the Reference Member State | Faramsil 400 microgram Prolonged-release Tablets  
Tamsulosin 400 microgram Prolonged-release Tablets |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of application</td>
<td>Generic (Article 10.1)</td>
</tr>
<tr>
<td>Name of the drug substance</td>
<td>Tamsulosin hydrochloride</td>
</tr>
<tr>
<td>Pharmacotherapeutic classification (ATC code)</td>
<td>Alpha adrenoceptor antagonist (G04CA02)</td>
</tr>
<tr>
<td>Pharmaceutical form and strength</td>
<td>Prolonged-release tablet, 400 microgram</td>
</tr>
</tbody>
</table>
| Reference numbers for the Decentralised Procedure   | UK/H/2481-2483/001/DC  
UK/H/4466-4467/001/DC |
| Reference Member State                              | United Kingdom                                                                                   |
| Member States concerned                             | UK/H/2481: BE, BG, CZ, DE, DK, FI, FR, NL, PL, PT, SI  
UK/H/2482: DE, LU  
UK/H/2483: CZ, DE, PL, PT  
UK/H/4466: LU  
UK/H/4467: LU |
| Start date of Decentralised Procedure               | 10 November 2008                                                                                 |
| End date of Decentralised Procedure                 | 9 June 2011                                                                                      |
| Marketing Authorisation numbers                     | PL 04416/0987-0989  
PL 04416/1220-1221 |
| Name and address of the Marketing Authorisation Holder | Sandoz Ltd  
Frimley Business Park, Frimley, Camberley, Surrey GU16 7SR  
UK |
Module 2

Summaries of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT
Faramsil 400 microgram Prolonged-release Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each film-coated prolonged-release tablet contains 0.4 mg tamsulosin hydrochloride.

Excipient(s):
Each film-coated prolonged-release tablet contains 18.75 mg lactose monohydrate.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Film-coated prolonged-release tablet

Round, bi-convex, brown film-coated tablet with debossing “0.4” on one side and “SZ” on the other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
Treatment of lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH).

4.2 Posology and method of administration
Posology
One tablet daily can be taken independently of food.

Method of administration
For oral use.
The tablet should be swallowed whole and should not be crushed or chewed as this will interfere with the prolonged release of the active ingredient.

Special populations
Renal impairment: no dose adjustment is required in patients with renal impairment
Hepatic impairment: no dose adjustment is required in patients with mild to moderate hepatic impairment (see also section 4.3)

Paediatric population
There is no relevant indication for the use of tamsulosin in the paediatric population.

4.3 **Contraindications**

Hypersensitivity to tamsulosin, including drug-induced angio-oedema, or to any of the excipients.

A history of orthostatic hypotension.

Severe hepatic insufficiency.

4.4 **Special warnings and precautions for use**

As with other alpha1-blockers, a reduction in blood pressure can occur in individual cases during treatment with tamsulosin, leading in rare cases to syncope. At the first signs of orthostatic hypotension (dizziness, weakness), the patient should sit or lie down until the symptoms have disappeared.

Prior to commencement of therapy with tamsulosin, the patient should be examined in order to exclude the presence of other conditions which may produce similar symptoms to those of benign prostatic hyperplasia. Digital rectal examination and, when necessary, determination of prostate specific antigen (PSA) should be performed prior to commencement of treatment and at regular intervals afterwards.

The treatment of patients with severe renal impairment (creatinine clearance 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. IFIS may lead to increased procedural complications during the operation. The initiation of therapy with tamsulosin in patients scheduled for cataract surgery is not recommended.

Discontinuing tamsulosin 1-2 weeks prior to cataract surgery has been recommended, however the benefit and duration of stopping the therapy prior to cataract surgery has not yet been established.

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 prolonged-release tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

4.5 **Interaction with other medicinal products and other forms of interaction**

Interaction studies have only been performed in adults. No interactions have been seen when tamsulosin was given concomitantly with atenolol, enalapril or theophylline. Concomitant cimetidine increases and concomitant furosemide lowers plasma levels of tamsulosin, however, 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 chlormadinon. No interactions at the level of hepatic metabolism have been seen during in vitro studies with liver microsomal fractions (representative of the cytochrome P450-linked drug metabolising enzyme system), involving amitriptyline, salbutamol, glibenclamide and finasteride. Diclofenac and warfarin, however, may increase the elimination rate of tamsulosin. There is a theoretical risk of enhanced hypotensive effect when given concomitantly with drugs which may reduce blood pressure, including anaesthetic agents and other alpha1-adrenoreceptors antagonists.

### 4.6 Pregnancy and lactation
Not applicable, as tamsulosin is intended for male patients only.

### 4.7 Effects on ability to drive and use machines
No studies on the effects on the ability to drive and use machines have been performed. However patients should be aware of the fact that drowsiness, blurred vision, dizziness and syncope can occur.

### 4.8 Undesirable effects
Tamsulosin prolonged-release tablets were evaluated in two double-blind placebo controlled trials. Adverse events were mostly mild and their incidence was generally low. The most commonly reported ADR was abnormal ejaculation occurring in approximately 2% of patients.

Suspected adverse reactions reported with Tamsulosin prolonged release tablets or an alternative formulation of tamsulosin, were:

<table>
<thead>
<tr>
<th>Category</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nervous system disorders</td>
<td></td>
</tr>
<tr>
<td>Common</td>
<td>dizziness</td>
</tr>
<tr>
<td>Uncommon</td>
<td>headache</td>
</tr>
<tr>
<td>Rare</td>
<td>syncope</td>
</tr>
<tr>
<td>Cardiac disorders</td>
<td></td>
</tr>
<tr>
<td>Uncommon</td>
<td>palpitations</td>
</tr>
<tr>
<td>Vascular disorders</td>
<td></td>
</tr>
<tr>
<td>Uncommon</td>
<td>orthostatic hypotension</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td></td>
</tr>
<tr>
<td>Uncommon</td>
<td>rhinitis</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td></td>
</tr>
<tr>
<td>Uncommon</td>
<td>nausea, vomiting, constipation, diarrhoea</td>
</tr>
</tbody>
</table>
Skin and subcutaneous tissue disorders
Uncommon: rash, pruritus, urticaria
Rare: angioedema
Very rare: Stevens-Johnson syndrome

Reproductive system and breast disorders
Common: ejaculation disorders
Very rare: priapism

General disorders
Uncommon: asthenia

As with other alpha-blockers, drowsiness, blurred vision, dry mouth or oedema 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 reliably determined.

4.9 Overdose
Acute overdose with 5 mg tamsulosin hydrochloride has been reported. Acute hypotension (systolic blood pressure 70 mm Hg), vomiting and diarrhoea were observed, which were treated with fluid replacement and the patient was able to be discharged the same day. In case of acute hypotension occurring after overdose, cardiovascular support should be given. Blood pressure can be restored and heart rate brought back to normal by lying the patient down. If this is insufficient 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
Alpha adrenoceptor antagonists.
ATC code: G04C A02. 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, resulting in relaxation of the smooth muscle of the prostate, whereby tension is reduced.

**Pharmacodynamic effects**
Tamsulosin increases maximum urinary flow rate by reducing smooth muscle tension in the prostate and urethra, 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 tamsulosin.

**5.2 Pharmacokinetic properties**

**Absorption**
Tamsulosin administered as a prolonged-release tablet is absorbed from the intestine and its bioavailability is approximately 55-59%. A consistent slow release of tamsulosin is maintained over the whole pH range encountered in the gastro-intestinal tract with little fluctuation over 24 hours. The rate and extent of absorption of tamsulosin administered as a prolonged release-tablet is not affected by food intake.

Tamsulosin shows linear kinetics.

Following administration of a single dose of tamsulosin in fasting state, plasma levels of tamsulosin peak at a median time of 6 hours. At steady state, which is reached by day 4 of multiple dosing, plasma levels of tamsulosin peak at 4 to 6 hours in fasting and fed state. Peak plasma levels increase from approximately 6 ng/ml after the first dose to 11 ng/ml at steady state.

As a result of the prolonged release characteristics of the tablet the trough concentration of tamsulosin in plasma amounts to 40% of the peak plasma concentration under fasting and fed conditions.

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

**Distribution**
In male patients, tamsulosin is about 99% bound to plasma proteins and the volume of distribution is small (about 0.2l/kg).

**Metabolism**
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.

None of the metabolites are more active than the original compound.
Elimination
Tamsulosin and its metabolites are mainly excreted in the urine. The urinary recovery of unchanged drug is estimated to be about 4-6% of the dose, administered as a prolonged release tablet.

After a single dose of tamsulosin, and at steady state, elimination half-life of about 19 and 15 hours, respectively, has been measured.

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 clinically irrelevant. Tamsulosin showed no relevant genotoxic properties.

Increased incidences of proliferative changes of mammary glands of female rats and mice have been reported. These findings appeared to be related to hyperprolactinaemia and only occurred at high dose levels, are regarded as irrelevant.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core
Cellulose, microcrystalline
Hydroxypropylcellulose
Lactose monohydrate
Polyethylene oxide
Butylhydroxytoluene
Magnesium stearate
Silica, colloidal anhydrous

Tablet film-coating
Hypromellose
Hydroxypropylcellulose
Macrogol 400
Titanium dioxide (E 171)
Talc
Quinoline yellow (E 104)
Carmine (E 120)
Iron oxide, black (E 172)

6.2 Incompatibilities
Not applicable.
6.3 Shelf life
2 years

6.4 Special precautions for storage
Store in the original package.

6.5 Nature and contents of container
Aluminium//Aluminium blisters.

Pack sizes: 10, 14, 20, 28, 30, 50, 56, 60, 80, 90, 100 and 200 film-coated prolonged-release tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal
No special requirements.

7 MARKETING AUTHORISATION HOLDER
Sandoz Ltd
Frimley Business Park,
Frimley,
Camberley,
Surrey,
GU16 7SR.
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)
PL 04416/0987

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
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10 DATE OF REVISION OF THE TEXT
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4 CLINICAL PARTICULARS

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Treatment of lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH).

4.2 Posology and method of administration
Posology
One tablet daily can be taken independently of food.

Method of administration
For oral use.
The tablet should be swallowed whole and should not be crushed or chewed as this will interfere with the prolonged release of the active ingredient.

Special populations
Renal impairment: no dose adjustment is required in patients with renal impairment
Hepatic impairment: no dose adjustment is required in patients with mild to moderate hepatic impairment (see also section 4.3)

Paediatric population
There is no relevant indication for the use of tamsulosin in the paediatric population.
4.3 Contraindications
Hypersensitivity to tamsulosin, including drug-induced angio-oedema, or to any of the excipients.
A history of orthostatic hypotension.
Severe hepatic insufficiency.

4.4 Special warnings and precautions for use
As with other alpha1-blockers, a reduction in blood pressure can occur in individual cases during treatment with tamsulosin, leading in rare cases to syncope. At the first signs of orthostatic hypotension (dizziness, weakness), the patient should sit or lie down until the symptoms have disappeared.

Prior to commencement of therapy with tamsulosin, the patient should be examined in order to exclude the presence of other conditions which may produce similar symptoms to those of benign prostatic hyperplasia. Digital rectal examination and, when necessary, determination of prostate specific antigen (PSA) should be performed prior to commencement of treatment and at regular intervals afterwards.

The treatment of patients with severe renal impairment (creatinine clearance 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. IFIS may lead to increased procedural complications during the operation. The initiation of therapy with tamsulosin in patients scheduled for cataract surgery is not recommended.

Discontinuing tamsulosin 1-2 weeks prior to cataract surgery has been recommended, however the benefit and duration of stopping the therapy prior to cataract surgery has not yet been established.

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 prolonged-release tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

4.5 Interaction with other medicinal products and other forms of interaction
Interaction studies have only been performed in adults. No interactions have been seen when tamsulosin was given concomitantly with atenolol, enalapril or theophylline. Concomitant cimetidine increases and concomitant furosemide lowers plasma levels of tamsulosin, however, as levels remain within the normal range, posology need not be changed. *In vitro*, neither diazepam nor propranolol, trichlormethiazide, chlormadinon, amitryptiline, diclofenac, glibenclamide, simvastatin and warfarin change the free fraction of...
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4.6 Pregnancy and lactation
Not applicable, as tamsulosin is intended for male patients only.

4.7 Effects on ability to drive and use machines
No studies on the effects on the ability to drive and use machines have been performed. However patients should be aware of the fact that drowsiness, blurred vision, dizziness and syncope can occur.

4.8 Undesirable effects
Tamsulosin prolonged-release tablets were evaluated in two double-blind placebo controlled trials. Adverse events were mostly mild and their incidence was generally low. The most commonly reported ADR was abnormal ejaculation occurring in approximately 2% of patients.

Suspected adverse reactions reported with Tamsulosin prolonged release tablets or an alternative formulation of tamsulosin, were:

Common (≥1/100 to <1/10), Uncommon (≥1/1,000 to <1/100) Rare (≥1/10,000 to <1/1,000) and Very rare (<1/10,000), including isolated reports.

Nervous systems disorders
Common: dizziness
Uncommon: headache
Rare: syncope

Cardiac disorders
Uncommon: palpitations

Vascular disorders
Uncommon: orthostatic hypotension

Respiratory, thoracic and mediastinal disorders
Uncommon: rhinitis

Gastrointestinal disorders
Uncommon: nausea, vomiting, constipation, diarrhoea

Skin and subcutaneous tissue disorders
Uncommon: rash, pruritus, urticaria
Rare: angioedema
Very rare: Stevens-Johnson syndrome

Reproductive system and breast disorders
Common: ejaculation disorders
Very rare: priapism

General disorders
Uncommon: asthenia

As with other alpha-blockers, drowsiness, blurred vision, dry mouth or oedema 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).

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Acute overdose with 5 mg tamsulosin hydrochloride has been reported. Acute hypotension (systolic blood pressure 70 mm Hg), vomiting and diarrhoea were observed, which were treated with fluid replacement and the patient was able to be discharged the same day. In case of acute hypotension occurring after overdose, cardiovascular support should be given. Blood pressure can be restored and heart rate brought back to normal by lying the patient down. If this is insufficient then volume expanders, and when necessary, vaspressors 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.

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### 5.2 Pharmacokinetic properties

**Absorption**

Tamsulosin administered as a prolonged-release tablet is absorbed from the intestine and its bioavailability is approximately 55-59%. A consistent slow release of tamsulosin is maintained over the whole pH range encountered in the gastro-intestinal tract with little fluctuation over 24 hours. The rate and extent of absorption of tamsulosin administered as a prolonged release-tablet is not affected by food intake.

Tamsulosin shows linear kinetics.

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

**Distribution**

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

**Metabolism**

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.

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

**Elimination**

Tamsulosin and its metabolites are mainly excreted in the urine. The urinary recovery of unchanged drug is estimated to be about 4-6% of the dose, administered as a prolonged release tablet.
After a single dose of tamsulosin, and at steady state, elimination half-life of about 19 and 15 hours, respectively, has been measured.

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6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core
- Cellulose, microcrystalline
- Hydroxypropylcellulose
- Lactose monohydrate
- Polyethylene oxide
- Butylhydroxytoluene
- Magnesium stearate
- Silica, colloidal anhydrous

Tablet film-coating
- Hypromellose
- Hydroxypropylcellulose
- Macrogol 400
- Titanium dioxide (E 171)
- Talc
- Quinoline yellow (E 104)
- Carmine (E 120)
- Iron oxide, black (E 172)

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
2 years
6.4 Special precautions for storage
Store in the original package.

6.5 Nature and contents of container
Aluminium/Aluminium blisters.

Pack sizes: 14, 20, 28, 30, 49, 50, 56, 98 and 100 film-coated prolonged-release tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal
No special requirements.

7 MARKETING AUTHORISATION HOLDER
Sandoz Ltd
Frimley Business Park,
Frimley,
Camberley,
Surrey,
GU16 7SR.
United Kingdom

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Special populations
Renal impairment: no dose adjustment is required in patients with renal impairment
Hepatic impairment: no dose adjustment is required in patients with mild to moderate hepatic impairment (see also section 4.3)

Paediatric population
There is no relevant indication for the use of tamsulosin in the paediatric population
4.3 **Contraindications**
Hypersensitivity to tamsulosin, including drug-induced angio-oedema, or to any of the excipients.
A history of orthostatic hypotension.
Severe hepatic insufficiency.

4.4 **Special warnings and precautions for use**
As with other alpha1-blockers, a reduction in blood pressure can occur in individual cases during treatment with tamsulosin, leading in rare cases to syncope. At the first signs of orthostatic hypotension (dizziness, weakness), the patient should sit or lie down until the symptoms have disappeared.

Prior to commencement of therapy with tamsulosin, the patient should be examined in order to exclude the presence of other conditions which may produce similar symptoms to those of benign prostatic hyperplasia. Digital rectal examination and, when necessary, determination of prostate specific antigen (PSA) should be performed prior to commencement of treatment and at regular intervals afterwards.

The treatment of patients with severe renal impairment (creatinine clearance 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. IFIS may lead to increased procedural complications during the operation. The initiation of therapy with tamsulosin in patients scheduled for cataract surgery is not recommended.

Discontinuing tamsulosin 1-2 weeks prior to cataract surgery has been recommended, however the benefit and duration of stopping the therapy prior to cataract surgery has not yet been established.

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 prolonged-release tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

4.5 **Interaction with other medicinal products and other forms of interaction**
Interaction studies have only been performed in adults. No interactions have been seen when tamsulosin was given concomitantly with atenolol, enalapril or theophylline. Concomitant cimetidine increases and concomitant furosemide lowers plasma levels of tamsulosin, however, as levels remain within the normal range, posology need not be changed. *In vitro*, neither diazepam nor propranolol, trichlormethiazide, chloramadinon, amitryptyline, 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 chlormadinon. No interactions at the level of hepatic metabolism have been seen during in vitro studies with liver microsomal fractions (representative of the cytochrome P450-linked drug metabolising enzyme system), involving amitriptyline, salbutamol, glibenclamide and finasteride. Diclofenac and warfarin, however, may increase the elimination rate of tamsulosin. There is a theoretical risk of enhanced hypotensive effect when given concomitantly with drugs which may reduce blood pressure, including anaesthetic agents and other alpha1-adrenoceptors antagonists.

4.6 Pregnancy and lactation
Not applicable, as tamsulosin is intended for male patients only.

4.7 Effects on ability to drive and use machines
No studies on the effects on the ability to drive and use machines have been performed. However patients should be aware of the fact that drowsiness, blurred vision, dizziness and syncope can occur.

4.8 Undesirable effects
Tamsulosin prolonged-release tablets were evaluated in two double-blind placebo controlled trials. Adverse events were mostly mild and their incidence was generally low. The most commonly reported ADR was abnormal ejaculation occurring in approximately 2% of patients.

Suspected adverse reactions reported with Tamsulosin prolonged release tablets or an alternative formulation of tamsulosin, were:

Common (≥1/100 to <1/10), Uncommon (≥1/1,000 to <1/100) Rare (≥1/10,000 to <1/1,000) and Very rare (<1/10,000), including isolated reports.

Nervous systems disorders
Common: dizziness
Uncommon: headache
Rare: syncope

Cardiac disorders
Uncommon: palpitations

Vascular disorders
Uncommon: orthostatic hypotension

Respiratory, thoracic and mediastinal disorders
Uncommon: rhinitis

Gastrointestinal disorders
Uncommon: nausea, vomiting, constipation, diarrhoea

Skin and subcutaneous tissue disorders
Uncommon: rash, pruritus, urticaria
Rare: angioedema
Very rare: Stevens-Johnson syndrome

Reproductive system and breast disorders
Common: ejaculation disorders
Very rare: priapism

General disorders
Uncommon: asthenia

As with other alpha-blockers, drowsiness, blurred vision, dry mouth or oedema 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 reliably determined.

4.9 Overdose
Acute overdose with 5 mg tamsulosin hydrochloride has been reported. Acute hypotension (systolic blood pressure 70 mm Hg), vomiting and diarrhoea were observed, which were treated with fluid replacement and the patient was able to be discharged the same day. In case of acute hypotension occurring after overdose, cardiovascular support should be given. Blood pressure can be restored and heart rate brought back to normal by lying the patient down. If this is insufficient 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
Alpha adrenoceptor antagonists.
ATC code: G04C A02. 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, resulting in relaxation of the smooth muscle of the prostate, whereby tension is reduced.
Pharmacodynamic effects
Tamsulosin increases maximum urinary flow rate by reducing smooth muscle tension in the prostate and urethra, 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 tamsulosin.

5.2 Pharmacokinetic properties
Absorption
Tamsulosin administered as a prolonged-release tablet is absorbed from the intestine and its bioavailability is approximately 55-59%. A consistent slow release of tamsulosin is maintained over the whole pH range encountered in the gastro-intestinal tract with little fluctuation over 24 hours. The rate and extent of absorption of tamsulosin administered as a prolonged release-tablet is not affected by food intake.

Tamsulosin shows linear kinetics.

Following administration of a single dose of tamsulosin in fasting state, plasma levels of tamsulosin peak at a median time of 6 hours. At steady state, which is reached by day 4 of multiple dosing, plasma levels of tamsulosin peak at 4 to 6 hours in fasting and fed state. Peak plasma levels increase from approximately 6 ng/ml after the first dose to 11 ng/ml at steady state.

As a result of the prolonged release characteristics of the tablet the trough concentration of tamsulosin in plasma amounts to 40% of the peak plasma concentration under fasting and fed conditions.

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

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

Metabolism
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.

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

Elimination
Tamsulosin and its metabolites are mainly excreted in the urine. The urinary recovery of unchanged drug is estimated to be about 4-6% of the dose, administered as a prolonged release tablet.
After a single dose of tamsulosin, and at steady state, elimination half-life of about 19 and 15 hours, respectively, has been measured.

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 clinically irrelevant. Tamsulosin showed no relevant genotoxic properties.

Increased incidences of proliferative changes of mammary glands of female rats and mice have been reported. These findings appeared to be related to hyperprolactinaemia and only occurred at high dose levels, are regarded as irrelevant.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Tablet core
Cellulose, microcrystalline
Hydroxypropylcellulose
Lactose monohydrate
Polyethylene oxide
Butylhydroxytoluene
Magnesium stearate
Silica, colloidal anhydrous

Tablet film-coating
Hypromellose
Hydroxypropylcellulose
Macrogol 400
Titanium dioxide (E 171)
Talc
Quinoline yellow (E 104)
Carmine (E 120)
Iron oxide, black (E 172)

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
2 years
6.4 Special precautions for storage
Store in the original package.

6.5 Nature and contents of container
Aluminium//Aluminium blisters.

Pack sizes: 10, 14, 20, 28, 30, 50, 56, 60, 80, 90, 100 and 200 film-coated prolonged-release tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal
No special requirements.

7 MARKETING AUTHORISATION HOLDER
Sandoz Ltd
Frimley Business Park,
Frimley,
Camberley,
Surrey,
GU16 7SR.
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)
PL 04416/0989

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
14/07/2011

10 DATE OF REVISION OF THE TEXT
14/07/2011
1 **NAME OF THE MEDICINAL PRODUCT**
Tamsulosin 400 microgram Prolonged-release Tablets

2 **QUALITATIVE AND QUANTITATIVE COMPOSITION**
Each film-coated prolonged-release tablet contains 0.4 mg tamsulosin hydrochloride.

Excipient(s):
Each film-coated prolonged-release tablet contains 18.75 mg lactose monohydrate.

For a full list of excipients, see section 6.1.

3 **PHARMACEUTICAL FORM**
Film-coated prolonged-release tablet

Round, bi-convex, brown film-coated tablet with debossing “0.4” on one side and “SZ” on the other side.

4 **CLINICAL PARTICULARS**

4.1 **Therapeutic indications**
Treatment of lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH).

4.2 **Posology and method of administration**

**Posology**
One tablet daily can be taken independently of food.

**Method of administration**
For oral use.
The tablet should be swallowed whole and should not be crushed or chewed as this will interfere with the prolonged release of the active ingredient.

**Special populations**
Renal impairment: no dose adjustment is required in patients with renal impairment
Hepatic impairment: no dose adjustment is required in patients with mild to moderate hepatic impairment (see also section 4.3)

**Paediatric population**
There is no relevant indication for the use of tamsulosin in the paediatric population.
4.3 Contraindications
Hypersensitivity to tamsulosin, including drug-induced angio-oedema, or to any of the excipients.
A history of orthostatic hypotension.
Severe hepatic insufficiency.

4.4 Special warnings and precautions for use
As with other alpha1-blockers, a reduction in blood pressure can occur in individual cases during treatment with tamsulosin, leading in rare cases to syncope. At the first signs of orthostatic hypotension (dizziness, weakness), the patient should sit or lie down until the symptoms have disappeared.

Prior to commencement of therapy with tamsulosin, the patient should be examined in order to exclude the presence of other conditions which may produce similar symptoms to those of benign prostatic hyperplasia. Digital rectal examination and, when necessary, determination of prostate specific antigen (PSA) should be performed prior to commencement of treatment and at regular intervals afterwards.

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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. IFIS may lead to increased procedural complications during the operation. The initiation of therapy with tamsulosin in patients scheduled for cataract surgery is not recommended.

Discontinuing tamsulosin 1-2 weeks prior to cataract surgery has been recommended, however the benefit and duration of stopping the therapy prior to cataract surgery has not yet been established.

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 prolonged-release tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

4.5 Interaction with other medicinal products and other forms of interaction
Interaction studies have only been performed in adults. No interactions have been seen when tamsulosin was given concomitantly with atenolol, enalapril or theophylline. Concomitant cimetidine increases and concomitant furosemide lowers plasma levels of tamsulosin, however, as levels remain within the normal range, posology need not be changed. In vitro, neither diazepam nor propranolol, trichlormethiazide, chlormadinon, amitryptyline, diclofenac, glibenclamide, simvastatin and warfarin change the free fraction of
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4.6 Pregnancy and lactation
Not applicable, as tamsulosin is intended for male patients only.

4.7 Effects on ability to drive and use machines
No studies on the effects on the ability to drive and use machines have been performed. However patients should be aware of the fact that drowsiness, blurred vision, dizziness and syncope can occur.

4.8 Undesirable effects
Tamsulosin prolonged-release tablets were evaluated in two double-blind placebo controlled trials. Adverse events were mostly mild and their incidence was generally low. The most commonly reported ADR was abnormal ejaculation occurring in approximately 2% of patients.

Suspected adverse reactions reported with Tamsulosin prolonged release tablets or an alternative formulation of tamsulosin, were:

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Uncommon: headache
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5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Alpha adrenoceptor antagonists.
ATC code: G04C A02. 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, resulting in relaxation of the smooth muscle of the prostate, whereby tension is reduced.
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5.2 Pharmacokinetic properties
Absorption
Tamsulosin administered as a prolonged-release tablet is absorbed from the intestine and its bioavailability is approximately 55-59%. A consistent slow release of tamsulosin is maintained over the whole pH range encountered in the gastro-intestinal tract with little fluctuation over 24 hours. The rate and extent of absorption of tamsulosin administered as a prolonged release-tablet is not affected by food intake.

Tamsulosin shows linear kinetics.

Following administration of a single dose of tamsulosin in fasting state, plasma levels of tamsulosin peak at a median time of 6 hours. At steady state, which is reached by day 4 of multiple dosing, plasma levels of tamsulosin peak at 4 to 6 hours in fasting and fed state. Peak plasma levels increase from approximately 6 ng/ml after the first dose to 11 ng/ml at steady state.

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

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

Metabolism
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.

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

Elimination
Tamsulosin and its metabolites are mainly excreted in the urine. The urinary recovery of unchanged drug is estimated to be about 4-6% of the dose, administered as a prolonged release tablet.
After a single dose of tamsulosin, and at steady state, elimination half-life of about 19 and 15 hours, respectively, has been measured.

5.3 **Preclinical safety data**

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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 clinically irrelevant. Tamsulosin showed no relevant genotoxic properties.

Increased incidences of proliferative changes of mammary glands of female rats and mice have been reported. These findings appeared to be related to hyperprolactinaemia and only occurred at high dose levels, are regarded as irrelevant.

6 **PHARMACEUTICAL PARTICULARS**

6.1 **List of excipients**

*Tablet core*
- Cellulose, microcrystalline
- Hydroxypropylcellulose
- Lactose monohydrate
- Polyethylene oxide
- Butylhydroxytoluene
- Magnesium stearate
- Silica, colloidal anhydrous

*Tablet film-coating*
- Hypromellose
- Hydroxypropylcellulose
- Macrogol 400
- Titanium dioxide (E 171)
- Talc
- Quinoline yellow (E 104)
- Carmine (E 120)
- Iron oxide, black (E 172)

6.2 **Incompatibilities**

Not applicable.

6.3 **Shelf life**

2 years
6.4 **Special precautions for storage**
Store in the original package.

6.5 **Nature and contents of container**
Aluminium/Aluminium blisters.

Pack sizes: 10, 14, 20, 28, 30, 49, 50, 56, 60, 80, 90, 98, 100 and 200 film-coated prolonged-release tablets.

Not all pack sizes may be marketed.

6.6 **Special precautions for disposal**
No special requirements.

7 **MARKETING AUTHORISATION HOLDER**
Sandoz Ltd
Frimley Business Park,
Frimley,
Camberley,
Surrey,
GU16 7SR.
United Kingdom

8 **MARKETING AUTHORISATION NUMBER(S)**
PL 04416/1220

9 **DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**
14/07/2011

10 **DATE OF REVISION OF THE TEXT**
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1 NAME OF THE MEDICINAL PRODUCT
Tamsulosin 400 microgram Prolonged-release Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each film-coated prolonged-release tablet contains 0.4 mg tamsulosin hydrochloride.

Excipient(s):
Each film-coated prolonged-release tablet contains 18.75 mg lactose monohydrate.

For a full list of excipients, see section 6.1.

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Film-coated prolonged-release tablet

Round, bi-convex, brown film-coated tablet with debossing “0.4” on one side and “SZ” on the other side.

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
Treatment of lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH).

4.2 Posology and method of administration
Posology
One tablet daily can be taken independently of food.

Method of administration
For oral use.
The tablet should be swallowed whole and should not be crushed or chewed as this will interfere with the prolonged release of the active ingredient.

Special populations
Renal impairment: no dose adjustment is required in patients with renal impairment
Hepatic impairment: no dose adjustment is required in patients with mild to moderate hepatic impairment (see also section 4.3)

Paediatric population
There is no relevant indication for the use of tamsulosin in the paediatric population.
4.3 Contraindications
Hypersensitivity to tamsulosin, including drug-induced angio-oedema, or to any of the excipients.
A history of orthostatic hypotension.
Severe hepatic insufficiency.

4.4 Special warnings and precautions for use
As with other alpha1-blockers, a reduction in blood pressure can occur in individual cases during treatment with tamsulosin, leading in rare cases to syncope. At the first signs of orthostatic hypotension (dizziness, weakness), the patient should sit or lie down until the symptoms have disappeared.

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Uncommon: rhinitis

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Tamsulosin increases maximum urinary flow rate by reducing smooth muscle tension in the prostate and urethra, 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 tamsulosin.

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Tamsulosin administered as a prolonged-release tablet is absorbed from the intestine and its bioavailability is approximately 55-59%. A consistent slow release of tamsulosin is maintained over the whole pH range encountered in the gastro-intestinal tract with little fluctuation over 24 hours. The rate and extent of absorption of tamsulosin administered as a prolonged release-tablet is not affected by food intake.

Tamsulosin shows linear kinetics.

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

Metabolism
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.

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

Elimination
Tamsulosin and its metabolites are mainly excreted in the urine. The urinary recovery of unchanged drug is estimated to be about 4-6% of the dose, administered as a prolonged release tablet.
After a single dose of tamsulosin, and at steady state, elimination half-life of about 19 and 15 hours, respectively, has been measured.

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 clinically irrelevant. Tamsulosin showed no relevant genotoxic properties.

Increased incidences of proliferative changes of mammary glands of female rats and mice have been reported. These findings appeared to be related to hyperprolactinaemia and only occurred at high dose levels, are regarded as irrelevant.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

*Tablet core*
- Cellulose, microcrystalline
- Hydroxypropylcellulose
- Lactose monohydrate
- Polyethylene oxide
- Butylhydroxytoluene
- Magnesium stearate
- Silica, colloidal anhydrous

*Tablet film-coating*
- Hypromellose
- Hydroxypropylcellulose
- Macrogol 400
- Titanium dioxide (E 171)
- Talc
- Quinoline yellow (E 104)
- Carmine (E 120)
- Iron oxide, black (E 172)

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
2 years
6.4 Special precautions for storage
Store in the original package.

6.5 Nature and contents of container
Aluminium/Aluminium blisters.

Pack sizes: 10, 14, 20, 28, 30, 49, 50, 56, 60, 80, 90, 98, 100 and 200 film-coated prolonged-release tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal
No special requirements.

7 MARKETING AUTHORITY NAME
Sandoz Ltd
Frimley Business Park,
Frimley,
Camberley,
Surrey,
GU16 7SR.
United Kingdom

8 MARKETING AUTHORITY NUMBER(S)
PL 04416/1221

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
14/07/2011

10 DATE OF REVISION OF THE TEXT
14/07/2011
Module 3

Product Information Leaflets

PL 04416/0987:
PACKAGE LEAFLET: INFORMATION FOR THE USER
Faramsil 400 microgram Prolonged-release Tablets

Read all of this leaflet carefully before you start taking this medicine.
- 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. Do not pass it on to others. It may harm them,
even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet,
please tell your doctor or pharmacist.

In this leaflet:
1. What Faramsil is and what it is used for
2. Before you take Faramsil
3. How to take Faramsil
4. Possible side effects
5. How to store Faramsil
6. Further information

1. What Faramsil is and what it is used for

Faramsil contains an active substance tamsulosin hydrochloride, which belongs to a group of medicines
called alpha-adrenoceptor blockers.

Faramsil relaxes:
- the muscles in the prostate gland,
- the tube from the bladder to the outside (the urethra).

This lets urine pass more easily through the urethra, making it easier to urinate.

Faramsil is for men who have benign prostate enlargement (benign prostatic hyperplasia, BPH).
This is when the prostate gland increases in size. This can make it difficult to pass urine. This means
you may have to pass urine often or during the night. You may also feel that you still need to pass urine
even after having done so. You may also dribble after passing urine.

2. Before you take Faramsil

Do not take Faramsil if:
- you are allergic (hypersensitive) to tamsulosin or any of the other ingredients of Faramsil (see list in
section 6 'Further information')
- you have a serious liver problem
- you feel dizzy or faint when you suddenly sit or stand up

Take special care with Faramsil
If you have a serious kidney problem, you should consult your doctor, before taking Faramsil.
As with other medicines in the same group, dizziness can occur in individual cases, when taking
Faramsil.
If you feel weak or dizzy, when taking Faramsil, you should sit or lie down straight away until the
symptoms have disappeared.

Before you start taking Faramsil your doctor may need to examine you. This is to check that you do not
have another condition with the same symptoms as BPH. Your doctor may also use a blood test before
you start taking the medicine. These tests may continue afterwards, to see how the medicine is working.

If you are undergoing eye surgery because of cloudiness of the lens (cataract), please inform your
eye specialist that you are using or have previously used tamsulosin. The specialist can then take
appropriate precautions with respect to medication and surgical techniques to be used. Ask your doctor
whether or not you should postponed or temporarily stop taking this medicine when undergoing eye
surgery because of a cloudy lens.

Taking other medicines
Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including
medicines obtained without a prescription. In particular, tell them about the medicines that lower
your blood pressure.

3. How to take Faramsil

Always take Faramsil exactly as your doctor has told you. You should check with your doctor or pharmacist
if you are not sure. The usual dose is one tablet each day. It can be taken with or without food. Swallow the
tablet whole. Do not crush or chew it.

If you take more Faramsil than you should:
- Talk to your doctor or pharmacist or go to the nearest hospital straight away.
- Take this leaflet and any of the remaining tablets with you.

If you forget to take Faramsil
If you forget to take your Faramsil at your usual time, take it later the same day.
If you miss a whole day, just take your normal tablet the next day. Do not take an extra tablet to make up
for the one you missed.

Continued on the next page...
If you stop taking Faramsil
If you stop taking Faramsil your original symptoms may return. You should keep taking Faramsil as advised by your doctor, even if your symptoms have gone away. Always talk to your doctor if you are thinking about stopping taking this medicine.

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

4. Possible side effects

Like all medicines, Faramsil can cause side effects, although not everybody gets them.

You should contact your doctor immediately if you notice any of the following side effects (it may be an allergic reaction):
- itchy skin rash (urticaria)
- swollen feet, hands, lips, tongue or throat and difficulty breathing.

If you feel weak or dizzy when taking Faramsil, you should sit or lie down straight away until the symptoms have disappeared.

Common (affect more than 1 person in 100 and less than 1 person in 10):
- feeling dizzy
- ejaculation disorders (little or no semen)

Uncommon (affect more than 1 person in 1,000 and less than 1 person in 100):
- headache
- fast or uneven heart beat (palpitations)
- a fall in blood pressure on standing up which causes dizziness, light-headedness or fainting
- runny or blocked nose
- feeling sick or being sick
- diarrhoea or constipation
- allergic reactions (skin rash, itchy or inflamed skin)
- feeling weak.

Rare (affect 1 to 10 users in 10,000):
- itching
- itchy skin rash (urticaria) with swollen feet, hands, lips, tongue or throat and difficulty breathing. In this case, see a doctor immediately.

Very rare (affect less than 1 person in 10,000):
- long-lasting and painful erection (priapism), normally not during sexual activity
- serious illness with blistering of the skin, mouth, eyes and genitals (Stevens-Johnson syndrome)

Frequency not known (cannot be estimated from the available data):
- irregular heart beat, faster heart beat
- shortness of breath

As with other medicines that belong to the same group (alpha-blockers), Faramsil can also cause dryness, blurred vision, dry mouth or oedema.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. How to store Faramsil

Keep out of the reach and sight of children.

Do not use Faramsil 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.

Store in the original package.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Further information

What Faramsil contains
- The active substance is 0.4 mg tamsulosin hydrochloride.
- The other ingredients are:
  - Tablet core: cellulose, microcrystalline, hydroxypropyl cellulose, lactose monohydrate, polyethylene oxide, butylhydroxytoluene, magnesium stearate, silica, colloidal anhydrous
  - Tablet film-coating: hydroxypropyl cellulose, hydroxypropyl methyl cellulose, titanium dioxide (E171), talc, quinoline yellow (E104), camphor (E125), iron oxide, black (E172)

What Faramsil looks like and contents of the pack
Faramsil 400 microgram Prolonged-release Tablets are brown, round, bi-convex film-coated tablets marked “0.4” on one side and “SZ” on the other side.

Faramsil is packed in aluminium/aluminium blisters: 10, 14, 20, 28, 30, 50, 56, 60, 80, 90, 100 or 200 film-coated prolonged-release tablets. Not all pack sizes may be marketed.

Marketing Authorisation Holder
Sanofi Ltd., Finley Business Park, Finley, Camberley, Surrey, GU16 7SR, UK.

Manufacturer
Lek Pharmaceuticals d.d., Vodnonska 87, 1526 Ljubljana, Slovenia or
Lek Pharmaceuticals d.d., Trimanj 20, 9220 Lendava, Slovenia or
Sulakta Pharma GmbH, Otto-von-Guericke Allee 1, 39170 Barleben, Germany or
Sulakta Pharma GmbH, Disselstraase 5, 73239 Goringen, Germany or
Lek S.A., Ul Domaniewska 50C, 02-672 Warszawa, Poland.

This leaflet was last approved in 07/2011 (to be amended after approval).
The following text is the approved Product Information Leaflet (PIL) text for PL 04416/0988, PL 04416/0989, PL 04416/1220 and PL 04416/1221. No PIL mock-ups have been provided. In accordance with medicines legislation, the products shall not be marketed in the UK until approval of the PIL mock-ups has been obtained.

PL 04416/0988:

PACKAGE LEAFLET: INFORMATION FOR THE USER

Tamsulosin 400 microgram Prolonged-release Tablets

tamsulosin hydrochloride

Read all of this leaflet carefully before you start taking this medicine.
- 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. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What Tamsulosin is and what it is used for
2. Before you take Tamsulosin
3. How to take Tamsulosin
4. Possible side effects
5. How to store Tamsulosin
6. Further information

1. WHAT TAMSULOSIN IS AND WHAT IT IS USED FOR

Tamsulosin contains an active substance tamsulosin hydrochloride, which belongs to a group of medicines called alpha adrenoceptor blockers.

Tamsulosin relaxes:
- the muscles in the prostate gland, and
- the tube from the bladder to the outside (the urethra).
This lets urine pass more easily through the urethra, making it easier to urinate.

Tamsulosin is for men who have benign prostate enlargement (benign prostatic hyperplasia, BPH). This is when the prostate gland increases in size. This can make it difficult to pass urine. This means you may have to pass urine often or during the night. You may also feel that you still need to pass urine even after having done so. You may also dribble after passing urine.

2. BEFORE YOU TAKE TAMSULOSIN
Do not take Tamsulosin if
- you are allergic (hypersensitive) to tamsulosin or any of the other ingredients of Tamsulosin (see list in section 6 ‘Further information’)
- you have a serious liver problem
- you feel dizzy or faint when you suddenly sit or stand up

Take special care with Tamsulosin
If you have a serious kidney problem. You should consult your doctor, before taking tamsulosin.

As with other medicines in the same group, dizziness can occur in individual cases, when taking tamsulosin.
If you feel weak or dizzy, when taking tamsulosin, you should sit or lie down straight away until the symptoms have disappeared.

Before you start taking tamsulosin your doctor may need to examine you. This is to check that you do not have another condition with the same symptoms as BPH. Your doctor may also use a blood test before you start taking the medicine. These tests may continue afterwards, to see how the medicine is working.

If you are undergoing eye surgery because of cloudiness of the lens (cataract), please inform your eye specialist that you are using or have previously used tamsulosin. The specialist can then take appropriate precautions with respect to medication and surgical techniques to be used. Ask your doctor whether or not you should postpone or temporarily stop taking this medicine when undergoing eye surgery because of a cloudy lens.

Taking other medicines
Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. In particular, tell them about the medicines that lower your blood pressure.

Taking Tamsulosin with food and drink
Tamsulosin can be taken independently of food.

Pregnancy and breast-feeding
Not applicable, as tamsulosin is intended for male patients only.

Driving and using machines
No studies on the effects on the ability to drive and use machines have been performed. However you should be aware of the fact that drowsiness, blurred vision, dizziness and fainting can occur. If you feel weak or dizzy, do not drive or use machines.

Important information about some of the ingredients of Tamsulosin
Tamsulosin contains lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.
3. HOW TO TAKE TAMSSULOSIN

Always take Tamsulosin exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure. The usual dose is one tablet each day. It can be taken with or without food. Swallow the tablet whole. Do not crush or chew it.

If you take more Tamsulosin than you should
- Talk to your doctor or pharmacist or go to the nearest hospital straight away.
- Take this leaflet and any of the remaining tablets with you.
Taking too much Tamsulosin may make you feel dizzy or faint and cause headache.

If you forget to take Tamsulosin
If you forget to take your Tamsulosin at your usual time, take it later the same day.
If you miss a whole day, just take your normal tablet the next day. Do not take an extra tablet to make up for the one you missed.

If you stop taking Tamsulosin
If you stop taking Tamsulosin your original symptoms may return. You should keep taking Tamsulosin as advised by your doctor, even if your symptoms have gone away. Always talk to your doctor if you are thinking about stopping taking this medicine.

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

4. POSSIBLE SIDE EFFECTS

Like all medicines, Tamsulosin can cause side effects, although not everybody gets them. You should contact your doctor immediately if you notice any of the following side effects (it may be an allergic reaction):
- lumpy skin rash (urticaria)
- swollen feet, hands, lips, tongue or throat and difficulty breathing.

If you feel weak or dizzy, when taking tamsulosin, you should sit or lie down straight away until the symptoms have disappeared.

Common (affect more than 1 person in 100 and less than 1 person in 10):
- feeling dizzy
- ejaculation disorders (little or no semen)

Uncommon (affect more than 1 person in 1,000 and less than 1 person in 100):
- headache
- fast or uneven heart beat (palpitations)
- a fall in blood pressure on standing up which causes dizziness, light-headedness or fainting
- runny or blocked nose
- feeling sick or being sick
- diarrhoea or constipation
- allergic reactions (skin rash, itchy or inflamed skin)
— feeling weak

**Rare** (affect 1 to 10 users in 10,000):
- fainting
- lumpy skin rash (urticaria) with swollen feet, hands, lips, tongue or throat and difficulty breathing. In this case, see a doctor immediately.

**Very rare** (affect less than 1 person in 10,000):
- long-lasting and painful erection (priapism), normally not during sexual activity
- serious illness with blistering of the skin, mouth, eyes and genitals (Stevens-Johnson syndrome)

**Frequency not known** (cannot be estimated from the available data):
- irregular heart beat, faster heart beat
- shortness of breath

As with other medicines that belong to the same group (alpha-blockers), tamsulosin can also cause drowsiness, blurred vision, dry mouth or oedema.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

**5. HOW TO STORE TAMSULOSIN**

Keep out of the reach and sight of children.

Do not use Tamsulosin 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.

Store in the original package.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

**6. FURTHER INFORMATION**

**What Tamsulosin contains**

- The active substance is 0.4 mg tamsulosin hydrochloride.
- The other ingredients are:
- **Tablet core**: cellulose, microcrystalline, hydroxypropylecellulose, lactose monohydrate, polyethylene oxide, butylhydroxytoluene, magnesium stearate, silica, colloidal anhydrous
- **Tablet film-coating**: hypromellose, hydroxypropylecellulose, macrogol 400, titanium dioxide (E171), talc, quinoline yellow (E104), carmine (E120), iron oxide, black (E172)

**What Tamsulosin looks like and contents of the pack**
Tamsulosin 400 microgram Prolonged-release Tablets are brown, round, bi-convex film-coated tablets marked “0.4” on one side and “SZ” on the other side.

Tamsulosin is packed in aluminium/aluminium blisters: 14, 20, 28, 30, 49, 50, 56, 98 or 100 film-coated prolonged-release tablets. Not all pack sizes may be marketed.

**Marketing Authorisation Holder**
Sandoz Ltd
Frimley Business Park,
Frimley,
Camberley,
Surrey,
GU16 7SR.
United Kingdom

**Manufacturer**
Lek Pharmaceuticals d.d., Verovskova 57, 1526 Ljubljana, Slovenia or
Lek Pharmaceuticals d.d., Trimlini 2D, 9220 Lendava, Slovenia or
Salutas Pharma GmbH, Otto-von-Guericke Allee 1, 39179 Barleben, Germany or
Salutas Pharma GmbH, Dieselstrasse 5, 70839 Gerlingen, Germany or
Lek S.A., Ul. Domaniewska 50C, 02-672 Warszawa, Poland

**This leaflet was last approved in** 07/2011 (To be amended after approval)
PL 04416/0989:

PACKAGE LEAFLET: INFORMATION FOR THE USER

Tamsulosin 400 microgram Prolonged-release Tablets

tamsulosin hydrochloride

Read all of this leaflet carefully before you start taking this medicine.
- 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. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What Tamsulosin is and what it is used for
2. Before you take Tamsulosin
3. How to take Tamsulosin
4. Possible side effects
5. How to store Tamsulosin
6. Further information

1. WHAT TAMSULOSIN IS AND WHAT IT IS USED FOR

Tamsulosin contains an active substance tamsulosin hydrochloride, which belongs to a group of medicines called alpha adrenoceptor blockers.

Tamsulosin relaxes:
- the muscles in the prostate gland, and
- the tube from the bladder to the outside (the urethra).
This lets urine pass more easily through the urethra, making it easier to urinate.

Tamsulosin is for men who have benign prostate enlargement (benign prostatic hyperplasia, BPH). This is when the prostate gland increases in size. This can make it difficult to pass urine. This means you may have to pass urine often or during the night. You may also feel that you still need to pass urine even after having done so. You may also dribble after passing urine.

2. BEFORE YOU TAKE TAMSULOSIN

Do not take Tamsulosin if
- you are allergic (hypersensitive) to tamsulosin or any of the other ingredients of Tamsulosin (see list in section 6 ‘Further information’).
- you have a serious liver problem
- you feel dizzy or faint when you suddenly sit or stand up

**Take special care with Tamsulosin**
If you have a serious kidney problem. You should consult your doctor, before taking tamsulosin.

As with other medicines in the same group, dizziness can occur in individual cases, when taking tamsulosin.
If you feel weak or dizzy, when taking tamsulosin, you should sit or lie down straight away until the symptoms have disappeared.

Before you start taking tamsulosin your doctor may need to examine you. This is to check that you do not have another condition with the same symptoms as BPH. Your doctor may also use a blood test before you start taking the medicine. These tests may continue afterwards, to see how the medicine is working.

If you are undergoing eye surgery because of cloudiness of the lens (cataract), please inform your eye specialist that you are using or have previously used tamsulosin. The specialist can then take appropriate precautions with respect to medication and surgical techniques to be used. Ask your doctor whether or not you should postpone or temporarily stop taking this medicine when undergoing eye surgery because of a cloudy lens.

**Taking other medicines**
Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. In particular, tell them about the medicines that lower your blood pressure.

**Taking Tamsulosin with food and drink**
Tamsulosin can be taken independently of food.

**Pregnancy and breast-feeding**
Not applicable, as tamsulosin is intended for male patients only.

**Driving and using machines**
No studies on the effects on the ability to drive and use machines have been performed. However you should be aware of the fact that drowsiness, blurred vision, dizziness and fainting can occur. If you feel weak or dizzy, do not drive or use machines.

**Important information about some of the ingredients of Tamsulosin**
Tamsulosin contains lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. **HOW TO TAKE TAMSULOSIN**
Always take Tamsulosin exactly as your doctor has told you. You should check with your
doctor or pharmacist if you are not sure. The usual dose is one tablet each day. It can be taken
with or without food. Swallow the tablet whole. Do not crush or chew it.

**If you take more Tamsulosin than you should**
- Talk to your doctor or pharmacist or go to the nearest hospital straight away.
- Take this leaflet and any of the remaining tablets with you.
Taking too much Tamsulosin may make you feel dizzy or faint and cause headache.

**If you forget to take Tamsulosin**
If you forget to take your Tamsulosin at your usual time, take it later the same day.
If you miss a whole day, just take your normal tablet the next day. Do not take an extra tablet
to make up for the one you missed.

**If you stop taking Tamsulosin**
If you stop taking Tamsulosin your original symptoms may return. You should keep taking
Tamsulosin as advised by your doctor, even if your symptoms have gone away. Always talk
to your doctor if you are thinking about stopping taking this medicine.

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

**4. POSSIBLE SIDE EFFECTS**

Like all medicines, Tamsulosin can cause side effects, although not everybody gets them.
**You should contact your doctor immediately if you notice any of the following side
effects (it may be an allergic reaction):**
- lumpy skin rash (urticaria)
- swollen feet, hands, lips, tongue or throat and difficulty breathing.

**If you feel weak or dizzy, when taking tamsulosin, you should sit or lie down straight
away until the symptoms have disappeared.**

**Common** (affect more than 1 person in 100 and less than 1 person in 10):
- feeling dizzy
- ejaculation disorders (little or no semen)

**Uncommon** (affect more than 1 person in 1,000 and less than 1 person in 100):
- headache
- fast or uneven heart beat (palpitations)
- a fall in blood pressure on standing up which causes dizziness, light-headedness or fainting
- runny or blocked nose
- feeling sick or being sick
- diarrhoea or constipation
- allergic reactions (skin rash, itchy or inflamed skin)
- feeling weak
Rare (affect 1 to 10 users in 10,000):
- fainting
- lumpy skin rash (urticaria) with swollen feet, hands, lips, tongue or throat and difficulty breathing. In this case, see a doctor immediately.

Very rare (affect less than 1 person in 10,000):
- long-lasting and painful erection (priapism), normally not during sexual activity
- serious illness with blistering of the skin, mouth, eyes and genitals (Stevens-Johnson syndrome)

Frequency not known (cannot be estimated from the available data):
- irregular heart beat, faster heart beat
- shortness of breath

As with other medicines that belong to the same group (alpha-blockers), tamsulosin can also cause drowsiness, blurred vision, dry mouth or oedema.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE TAMSULOSIN

Keep out of the reach and sight of children.

Do not use Tamsulosin 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.

Store in the original package.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Tamsulosin contains

- The active substance is 0.4 mg tamsulosin hydrochloride.
- The other ingredients are:
- **Tablet core:** cellulose, microcrystalline, hydroxypropylcellulose, lactose monohydrate, polyethylene oxide, butylhydroxytoluene, magnesium stearate, silica, colloidal anhydrous
- **Tablet film-coating:** hypromellose, hydroxypropylcellulose, macrogol 400, titanium dioxide (E171), talc, quinoline yellow (E104), carmine (E120), iron oxide, black (E172)

**What Tamsulosin looks like and contents of the pack**
Tamsulosin 400 microgram Prolonged-release Tablets are brown, round, bi-convex film-coated tablets marked “0.4” on one side and “SZ” on the other side.

Tamsulosin is packed in aluminium/aluminium blisters: 10, 14, 20, 28, 30, 50, 56, 60, 80, 90, 100 or 200 film-coated prolonged-release tablets. Not all pack sizes may be marketed.

**Marketing Authorisation Holder**
Sandoz Ltd
Frimley Business Park,
Frimley,
Camberley,
Surrey,
GU16 7SR.
United Kingdom

**Manufacturer**
Lek Pharmaceuticals d.d., Verovskova 57, 1526 Ljubljana, Slovenia or

Lek Pharmaceuticals d.d., Trimlini 2D, 9220 Lendava, Slovenia or

Salutas Pharma GmbH, Otto-von-Guericke Allee 1, 39179 Barleben, Germany or

Salutas Pharma GmbH, Dieselstrasse 5, 70839 Gerlingen, Germany or

Lek S.A., Ul. Domaniewska 50C, 02-672 Warszawa, Poland

**This leaflet was last approved in** 07/2011 (To be amended after approval)
PL 04416/1220:

Tamsulosin 400 microgram Prolonged-release Tablets

tamsulosin hydrochloride

Read all of this leaflet carefully before you start taking this medicine.
- 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. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What Tamsulosin is and what it is used for
2. Before you take Tamsulosin
3. How to take Tamsulosin
4. Possible side effects
5. How to store Tamsulosin
6. Further information

1. WHAT TAMSULOSIN IS AND WHAT IT IS USED FOR

Tamsulosin contains an active substance tamsulosin hydrochloride, which belongs to a group of medicines called alpha adrenoceptor blockers.

Tamsulosin relaxes:
- the muscles in the prostate gland, and
- the tube from the bladder to the outside (the urethra).
This lets urine pass more easily through the urethra, making it easier to urinate.

Tamsulosin is for men who have benign prostate enlargement (benign prostatic hyperplasia, BPH). This is when the prostate gland increases in size. This can make it difficult to pass urine. This means you may have to pass urine often or during the night. You may also feel that you still need to pass urine even after having done so. You may also dribble after passing urine.

2. BEFORE YOU TAKE TAMSULOSIN

Do not take Tamsulosin if
- you are allergic (hypersensitive) to tamsulosin or any of the other ingredients of Tamsulosin (see list in section 6 'Further information')
- you have a serious liver problems
- you feel dizzy or faint when you suddenly sit or stand up

**Take special care with Tamsulosin**

If you have a serious kidney problem. You should consult your doctor, before taking tamsulosin.

As with other medicines in the same group, dizziness can occur in individual cases, when taking tamsulosin.

If you feel weak or dizzy, when taking tamsulosin, you should sit or lie down straight away until the symptoms have disappeared.

Before you start taking tamsulosin your doctor may need to examine you. This is to check that you do not have another condition with the same symptoms as BPH. Your doctor may also use a blood test before you start taking the medicine. These tests may continue afterwards, to see how the medicine is working.

If you are undergoing eye surgery because of cloudiness of the lens (cataract), please inform your eye specialist that you are using or have previously used tamsulosin. The specialist can then take appropriate precautions with respect to medication and surgical techniques to be used. Ask your doctor whether or not you should postpone or temporarily stop taking this medicine when undergoing eye surgery because of a cloudy lens.

**Taking other medicines**

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. In particular, tell them about the medicines that lower your blood pressure.

**Taking Tamsulosin with food and drink**

Tamsulosin can be taken independently of food.

**Pregnancy and breast-feeding**

Not applicable, as tamsulosin is intended for male patients only.

**Driving and using machines**

No studies on the effects on the ability to drive and use machines have been performed. However you should be aware of the fact that drowsiness, blurred vision, dizziness and fainting can occur. If you feel weak or dizzy, do not drive or use machines.

**Important information about some of the ingredients of Tamsulosin**

Tamsulosin contains lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.
3. HOW TO TAKE TAMSULOSIN

Always take Tamsulosin exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure. The usual dose is one tablet each day. It can be taken with or without food. Swallow the tablet whole. Do not crush or chew it.

If you take more Tamsulosin than you should
- Talk to your doctor or pharmacist or go to the nearest hospital straight away.
- Take this leaflet and any of the remaining tablets with you.
Taking too much Tamsulosin may make you feel dizzy or faint and cause headache.

If you forget to take Tamsulosin
If you forget to take your Tamsulosin at your usual time, take it later the same day.
If you miss a whole day, just take your normal tablet the next day. Do not take an extra tablet to make up for the one you missed.

If you stop taking Tamsulosin
If you stop taking Tamsulosin your original symptoms may return. You should keep taking Tamsulosin as advised by your doctor, even if your symptoms have gone away. Always talk to your doctor if you are thinking about stopping taking this medicine.

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

4. POSSIBLE SIDE EFFECTS

Like all medicines, Tamsulosin can cause side effects, although not everybody gets them.

You should contact your doctor immediately if you notice any of the following side effects (it may be an allergic reaction):
- lumpy skin rash (urticaria)
- swollen feet, hands, lips, tongue or throat and difficulty breathing.

If you feel weak or dizzy, when taking tamsulosin, you should sit or lie down straight away until the symptoms have disappeared.

Common (affect more than 1 person in 100 and less than 1 person in 10):
- feeling dizzy
- ejaculation disorders (little or no semen)

Uncommon (affect more than 1 person in 1,000 and less than 1 person in 100):
- headache
- fast or uneven heart beat (palpitations)
- a fall in blood pressure on standing up which causes dizziness, light-headedness or fainting
- runny or blocked nose
- feeling sick or being sick
- diarrhoea or constipation
- allergic reactions (skin rash, itchy or inflamed skin)
- feeling weak

**Rare** (affect 1 to 10 users in 10,000):
- fainting
- lumpy skin rash (urticaria) with swollen feet, hands, lips, tongue or throat and difficulty breathing. In this case, see a doctor immediately.

**Very rare** (affect less than 1 person in 10,000):
- long-lasting and painful erection (priapism), normally not during sexual activity
- serious illness with blistering of the skin, mouth, eyes and genitals (Stevens-Johnson syndrome)

**Frequency not known** (cannot be estimated from the available data):
- irregular heart beat, faster heart beat
- shortness of breath

As with other medicines that belong to the same group (alpha-blockers), tamsulosin can also cause drowsiness, blurred vision, dry mouth or oedema.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

**5. HOW TO STORE TAMSULOSIN**

Keep out of the reach and sight of children.

Do not use Tamsulosin 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.

Store in the original package.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

**6. FURTHER INFORMATION**

What Tamsulosin contains
- The active substance is 0.4 mg tamsulosin hydrochloride.
- The other ingredients are:
  - *Tablet core*: cellulose, microcrystalline, hydroxypropylcellulose, lactose monohydrate, polyethylene oxide, butylhydroxytoluene, magnesium stearate, silica, colloidal anhydrous
  - *Tablet film-coating*: hypromellose, hydroxypropylcellulose, macrogol 400, titanium dioxide (E171), talc, quinoline yellow (E104), carmine (E120), iron oxide, black (E172)

**What Tamsulosin looks like and contents of the pack**

Tamsulosin 400 microgram Prolonged-release Tablets are brown, round, bi-convex film-coated tablets marked “0.4” on one side and “SZ” on the other side.

Tamsulosin is packed in aluminium/aluminium blisters: 10, 14, 20, 28, 30, 49, 50, 56, 60, 80, 90, 98, 100 and 200 film-coated prolonged-release tablets. Not all pack sizes may be marketed.

**Marketing Authorisation Holder**

Sandoz Ltd
Frimley Business Park,
Frimley,
Camberley,
Surrey,
GU16 7SR,
United Kingdom

**Manufacturer**

Lek Pharmaceuticals d.d., Verovskova 57, 1526 Ljubljana, Slovenia or

Lek Pharmaceuticals d.d., Trimlini 2D, 9220 Lendava, Slovenia or

Salutas Pharma GmbH, Otto-von-Guericke Allee 1, 39179 Barleben, Germany or

Salutas Pharma GmbH, Dieselstrasse 5, 70839 Gerlingen, Germany or

Lek S.A., Ul. Domanięwska 50C, 02- 672 Warszawa, Poland

**This leaflet was last approved in** 07/2011 (To be amended after approval)
PL 04416/1221:

PACKAGE LEAFLET: INFORMATION FOR THE USER

Tamsulosin 400 microgram Prolonged-release Tablets

tamsulosin hydrochloride

Read all of this leaflet carefully before you start taking this medicine.
- 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. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What Tamsulosin is and what it is used for
2. Before you take Tamsulosin
3. How to take Tamsulosin
4. Possible side effects
5. How to store Tamsulosin
6. Further information

1. WHAT TAMSULOSIN IS AND WHAT IT IS USED FOR

Tamsulosin contains an active substance tamsulosin hydrochloride, which belongs to a group of medicines called alpha adrenoceptor blockers.

Tamsulosin relaxes:
- the muscles in the prostate gland, and
- the tube from the bladder to the outside (the urethra).
This lets urine pass more easily through the urethra, making it easier to urinate.

Tamsulosin is for men who have benign prostate enlargement (benign prostatic hyperplasia, BPH). This is when the prostate gland increases in size. This can make it difficult to pass urine. This means you may have to pass urine often or during the night. You may also feel that you still need to pass urine even after having done so. You may also dribble after passing urine.

2. BEFORE YOU TAKE TAMSULOSIN

Do not take Tamsulosin if
- you are allergic (hypersensitive) to tamsulosin or any of the other ingredients of Tamsulosin (see list in section 6 ‘Further information’)
- you have a serious liver problems
- you feel dizzy or faint when you suddenly sit or stand up

**Take special care with Tamsulosin**
If you have a serious kidney problem. You should consult your doctor, before taking tamsulosin.

As with other medicines in the same group, dizziness can occur in individual cases, when taking tamsulosin.

If you feel weak or dizzy, when taking tamsulosin, you should sit or lie down straight away until the symptoms have disappeared.

Before you start taking tamsulosin your doctor may need to examine you. This is to check that you do not have another condition with the same symptoms as BPH. Your doctor may also use a blood test before you start taking the medicine. These tests may continue afterwards, to see how the medicine is working.

If you are undergoing eye surgery because of cloudiness of the lens (cataract), please inform your eye specialist that you are using or have previously used tamsulosin. The specialist can then take appropriate precautions with respect to medication and surgical techniques to be used. Ask your doctor whether or not you should postpone or temporarily stop taking this medicine when undergoing eye surgery because of a cloudy lens.

**Taking other medicines**
Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. In particular, tell them about the medicines that lower your blood pressure.

**Taking Tamsulosin with food and drink**
Tamsulosin can be taken independently of food.

**Pregnancy and breast-feeding**
Not applicable, as tamsulosin is intended for male patients only.

**Driving and using machines**
No studies on the effects on the ability to drive and use machines have been performed. However you should be aware of the fact that drowsiness, blurred vision, dizziness and fainting can occur. If you feel weak or dizzy, do not drive or use machines.

**Important information about some of the ingredients of Tamsulosin**
Tamsulosin contains lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

**3. HOW TO TAKE TAMSULOSIN**
Always take Tamsulosin exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure. The usual dose is one tablet each day. It can be taken with or without food. Swallow the tablet whole. Do not crush or chew it.

**If you take more Tamsulosin than you should**
- Talk to your doctor or pharmacist or go to the nearest hospital straight away.
- Take this leaflet and any of the remaining tablets with you.
Taking too much Tamsulosin may make you feel dizzy or faint and cause headache.

**If you forget to take Tamsulosin**
If you forget to take your Tamsulosin at your usual time, take it later the same day. If you miss a whole day, just take your normal tablet the next day. Do not take an extra tablet to make up for the one you missed.

**If you stop taking Tamsulosin**
If you stop taking Tamsulosin your original symptoms may return. You should keep taking Tamsulosin as advised by your doctor, even if your symptoms have gone away. Always tell your doctor if you are thinking about stopping taking this medicine.

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

**4. POSSIBLE SIDE EFFECTS**

Like all medicines, Tamsulosin can cause side effects, although not everybody gets them.

**You should contact your doctor immediately if you notice any of the following side effects (it may be an allergic reaction):**
- lumpy skin rash (urticaria)
- swollen feet, hands, lips, tongue or throat and difficulty breathing.

**If you feel weak or dizzy, when taking tamsulosin, you should sit or lie down straight away until the symptoms have disappeared.**

**Common** (affect more than 1 person in 100 and less than 1 person in 10):
- feeling dizzy
- ejaculation disorders (little or no semen)

**Uncommon** (affect more than 1 person in 1,000 and less than 1 person in 100):
- headache
- fast or uneven heart beat (palpitations)
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- feeling sick or being sick
- diarrhoea or constipation
- allergic reactions (skin rash, itchy or inflamed skin)
feeling weak

**Rare** (affect 1 to 10 users in 10,000):
- fainting
- lumpy skin rash (urticaria) with swollen feet, hands, lips, tongue or throat and difficulty breathing. In this case, see a doctor immediately.

**Very rare** (affect less than 1 person in 10,000):
- long-lasting and painful erection (priapism), normally not during sexual activity
- serious illness with blistering of the skin, mouth, eyes and genitals (Stevens-Johnson syndrome)

**Frequency not known** (cannot be estimated from the available data):
- irregular heart beat, faster heart beat
- shortness of breath

As with other medicines that belong to the same group (alpha-blockers), tamsulosin can also cause drowsiness, blurred vision, dry mouth or oedema.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. **HOW TO STORE TAMSULOSIN**

Keep out of the reach and sight of children.

Do not use Tamsulosin 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.

Store in the original package.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. **FURTHER INFORMATION**

**What Tamsulosin contains**

- The active substance is 0.4 mg tamsulosin hydrochloride.
- The other ingredients are:
- **Tablet core**: cellulose, microcrystalline, hydroxypropylecellulose, lactose monohydrate, polyethylene oxide, butylhydroxytoluene, magnesium stearate, silica, colloidal anhydrous
- **Tablet film-coating**: hypromellose, hydroxypropylecellulose, macrogol 400, titanium dioxide (E171), talc, quinoline yellow (E104), carmine (E120), iron oxide, black (E172)

**What Tamsulosin looks like and contents of the pack**
Tamsulosin 400 microgram Prolonged-release Tablets are brown, round, bi-convex film-coated tablets marked “0.4” on one side and “SZ” on the other side.

Tamsulosin is packed in aluminium/aluminium blisters: 10, 14, 20, 28, 30, 49, 50, 56, 60, 80, 90, 98, 100 or 200 film-coated prolonged-release tablets. Not all pack sizes may be marketed.

**Marketing Authorisation Holder**
Sandoz Ltd
Frimley Business Park,
Frimley,
Camberley,
Surrey,
GU16 7SR.
United Kingdom

**Manufacturer**
Lek Pharmaceuticals d.d., Verovskova 57, 1526 Ljubljana, Slovenia or
Lek Pharmaceuticals d.d., Trimlini 2D, 9220 Lendava, Slovenia or
Salutas Pharma GmbH, Otto-von-Guericke Allee 1, 39179 Barleben, Germany or
Salutas Pharma GmbH, Dieselstrasse 5, 70839 Gerlingen, Germany or
Lek S.A., Ul. Domaniewska 50C, 02- 672 Warszawa, Poland.

This leaflet was last approved in 07/2011 (To be amended after approval)
Module 4

Labelling

PL 04416/0987:
Blisters:
The following text is the approved label text for PL 04416/0988, PL 04416/0989, PL 04416/1220 and PL 04416/1221. No label mock-ups have been provided. In accordance with medicines legislation, the products shall not be marketed in the UK until approval of the label mock-ups has been obtained.

**PL 04416/0988:**

<table>
<thead>
<tr>
<th>PARTICULARS TO APPEAR ON THE OUTER PACKAGING OR, WHERE THERE IS NO OUTER PACKAGING, ON THE IMMEDIATE PACKAGING</th>
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<tbody>
<tr>
<td>Carton box</td>
</tr>
</tbody>
</table>

**1. NAME OF THE MEDICINAL PRODUCT**

Tamsulosin 400 microgram Prolonged-release Tablets
Tamsulosin hydrochloride

**2. STATEMENT OF ACTIVE SUBSTANCE(S)**

Each film-coated prolonged-release tablet contains 0.4 mg tamsulosin hydrochloride

**3. LIST OF EXCIPIENTS**

Contains lactose monohydrate

See leaflet for further information

**4. PHARMACEUTICAL FORM AND CONTENTS**

Film-coated prolonged-release tablet

| 14 film-coated prolonged-release tablets |
| 20 film-coated prolonged-release tablets |
| 28 film-coated prolonged-release tablets |
| 30 film-coated prolonged-release tablets |
| 49 film-coated prolonged-release tablets |
| 50 film-coated prolonged-release tablets |
| 56 film-coated prolonged-release tablets |
| 98 film-coated prolonged-release tablets |
| 100 film-coated prolonged-release tablets |

**5. METHOD AND ROUTE(S) OF ADMINISTRATION**

Read the package leaflet before use
For oral use
Swallow whole, do not crunch or chew
6. **SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN**

Keep out of the reach and sight of children.

7. **OTHER SPECIAL WARNING(S), IF NECESSARY**

8. **EXPIRY DATE**

EXP

9. **SPECIAL STORAGE CONDITIONS**

Store in the original package

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**

Sandoz Limited
Frimley Business Park
Frimley
Camberley
Surrey
GU16 7SR

12. **MARKETING AUTHORISATION NUMBER(S)**

PL 04416/0988

13. **MANUFACTURER’S BATCH NUMBER**

Lot

14. **GENERAL CLASSIFICATION FOR SUPPLY**

POM

15. **INSTRUCTIONS ON USE**

Use as directed by your doctor
<table>
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<tr>
<th>16. INFORMATION IN BRAILLE</th>
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<tbody>
<tr>
<td>Tamsulosin 400 microgram Prolonged-release Tablets</td>
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<tr>
<th>MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS</th>
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<td>Aluminium//Aluminium blister</td>
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<th>1. NAME OF THE MEDICINAL PRODUCT</th>
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<th>5. OTHER</th>
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PL 04416/0989:

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING OR, WHERE THERE IS NO OUTER PACKAGING, ON THE IMMEDIATE PACKAGING**

Carton box

**1. NAME OF THE MEDICINAL PRODUCT**

Tamsulosin 400 microgram Prolonged-release Tablets
Tamsulosin hydrochloride

**2. STATEMENT OF ACTIVE SUBSTANCE(S)**

Each film-coated prolonged-release tablet contains 0.4 mg tamsulosin hydrochloride

**3. LIST OF EXCIPIENTS**

Contains lactose monohydrate

See leaflet for further information

**4. PHARMACEUTICAL FORM AND CONTENTS**

Film-coated prolonged-release tablet

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<th>Quantity</th>
<th>Description</th>
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<td>200</td>
<td>film-coated prolonged-release tablets</td>
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</tbody>
</table>

**5. METHOD AND ROUTE(S) OF ADMINISTRATION**

Read the package leaflet before use
For oral use
6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in the original package

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 AUTHORIZATION HOLDER

Sandoz Limited
Frimley Business Park
Frimley
Camberley
Surrey
GU16 7SR

12. MARKETING AUTHORIZATION NUMBER(S)

PL 04416/0989

13. MANUFACTURER’S BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

POM

15. INSTRUCTIONS ON USE
16. INFORMATION IN BRAILLE
Tamsulosin 400 microgram Prolonged-release Tablets

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS
Aluminium//Aluminium blister

1. NAME OF THE MEDICINAL PRODUCT
Tamsulosin 400 microgram Prolonged-release Tablets
Tamsulosin hydrochloride

2. NAME OF THE MARKETING AUTHORISATION HOLDER
Sandoz Limited

3. EXPIRY DATE
EXP

4. BATCH NUMBER
Lot

5. OTHER
PL 04416/1220:

1. **NAME OF THE MEDICINAL PRODUCT**

   Tamsulosin 400 microgram Prolonged-release Tablets
   Tamsulosin hydrochloride

2. **STATEMENT OF ACTIVE SUBSTANCE(S)**

   Each film-coated prolonged-release tablet contains 0.4 mg tamsulosin hydrochloride

3. **LIST OF EXCIPIENTS**

   Contains lactose monohydrate

   See leaflet for further information

4. **PHARMACEUTICAL FORM AND CONTENTS**

<table>
<thead>
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<th>Film-coated prolonged-release tablet</th>
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5. **METHOD AND ROUTE(S) OF ADMINISTRATION**

   Read the package leaflet before use

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

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

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Store in the original package

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PL 04416/1220

13. MANUFACTURER’S BATCH NUMBER

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15. INSTRUCTIONS ON USE

Use as directed by your doctor

16. INFORMATION IN BRAILLE

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1. NAME OF THE MEDICINAL PRODUCT

Tamsulosin 400 microgram Prolonged-release Tablets
Tamsulosin hydrochloride

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Sandoz Limited

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER
PL 04416/1221:

1. **NAME OF THE MEDICINAL PRODUCT**

Tamsulosin 400 microgram Prolonged-release Tablets
Tamsulosin hydrochloride

2. **STATEMENT OF ACTIVE SUBSTANCE(S)**

Each film-coated prolonged-release tablet contains 0.4 mg tamsulosin hydrochloride

3. **LIST OF EXCIPIENTS**

Contains lactose monohydrate

See leaflet for further information

4. **PHARMACEUTICAL FORM AND CONTENTS**

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<td>Swallow whole, do not crunch or chew</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Keep out of the reach and sight of children.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>7. OTHER SPECIAL WARNING(S), IF NECESSARY</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>8. EXPIRY DATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>EXP</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>9. SPECIAL STORAGE CONDITIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Store in the original package</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sandoz Limited</td>
</tr>
<tr>
<td>Frimley Business Park</td>
</tr>
<tr>
<td>Frimley</td>
</tr>
<tr>
<td>Camberley</td>
</tr>
<tr>
<td>Surrey</td>
</tr>
<tr>
<td>GU16 7SR</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>12. MARKETING AUTHORISATION NUMBER(S)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PL 04416/1221</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>13. MANUFACTURER’S BATCH NUMBER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lot</td>
</tr>
</tbody>
</table>
**14. GENERAL CLASSIFICATION FOR SUPPLY**

POM

**15. INSTRUCTIONS ON USE**

Use as directed by your doctor

**16. INFORMATION IN BRAILLE**

Tamsulosin 400 microgram Prolonged-release Tablets

**MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS**

Aluminium//Aluminium blister

**1. NAME OF THE MEDICINAL PRODUCT**

Tamsulosin 400 microgram Prolonged-release Tablets
Tamsulosin hydrochloride

**2. NAME OF THE MARKETING AUTHORISATION HOLDER**

Sandoz Limited

**3. EXPIRY DATE**

EXP

**4. BATCH NUMBER**

Lot

**5. OTHER**
Module 5

Scientific Discussion

RECOMMENDATION
Based on the review of the data on quality, safety and efficacy, the RMS considers that the applications for Faramsil 400 microgram Prolonged-release Tablets (PL 04416/0987) and Tamsulosin 400 microgram Prolonged-release Tablets (PL 04416/0988-0989 and PL 04416/1220-1221) in the symptomatic treatment of benign prostate hyperplasia could be approved.

EXECUTIVE SUMMARY

Problem statement
These Decentralised applications were submitted under Article 10.1 of Directive 2001/83/EC, as amended. The applicant claims that the proposed products are generic versions of the product Flomax MR, 400 micrograms, prolonged release tablets (PL 00166/0171), which has been licensed in the UK to Astellas Pharma Ltd since 16 April 1996. The reference product has, therefore, been authorised in the EEA for at least 10 years and the legal basis of these applications is acceptable.

With the UK as the Reference Member State in this Decentralised Procedure, Sandoz Ltd is applying for Marketing Authorisations for these products in the following Concerned Member States:

UK/H/2481/001/DC: BE, BG, CZ, DE, DK, FI, FR, NL, PL, PT, SI
UK/H/2482/001/DC: DE, LU
UK/H/2483/001/DC: CZ, DE, PL, PT
UK/H/4466/001/DC: LU
UK/H/4467/001/DC: LU

About the products
Tamsulosin is an alpha l-adrenoceptor antagonist. It binds selectively and competitively to postsynaptic alpha l-receptors, in particular to the subtype alpha 1a, which bring about relaxation of the smooth muscle of the prostate, whereby tension is reduced. It increases maximum urinary flow rate by reducing smooth muscle tension in the prostate and urethra and thereby relieving obstruction.

General comments on the submitted dossier
The submitted documentation in relation to the proposed type of product is considered to be of sufficient quality and is consistent with the current EU regulatory requirements. Satisfactory overall summaries of the dossier regarding the quality, preclinical and clinical parts have been submitted.

General comments on compliance with GMP, GLP, GCP and agreed ethical principles

GMP
The RMS has been assured that acceptable standards of GMP are in place for these
product types at all sites responsible for the manufacture and assembly of these products.

For manufacturing sites within the Community, the RMS has accepted copies of current manufacturer authorisations issued by inspection services of the competent authorities as certification that acceptable standards of GMP are in place at those sites.

**GLP**

No new preclinical studies were submitted in support of these applications, and none are needed for an application of this type.

**GCP**

Statements have been provided confirming that the submitted bioequivalence study was conducted in compliance with Good Clinical Practices (GCP), as referenced in the ICH guidelines (ICH E6), local regulatory requirements, and the principles enunciated in the Declaration of Helsinki.

**SCIENTIFIC OVERVIEW AND DISCUSSION**

**Quality aspects**

**Drug substance**

INN: Tamsulosin hydrochloride

Chemical names: 5-[(2R)-2-[2-2(ethoxyphenoxy)ethyl]amino]propyl]-2-methoxybenzenesulfonamide hydrochloride

**Structure**

![Chemical structure of Tamsulosin hydrochloride]

**General Properties**

Description: White or almost white powder

Molecular formula: C$_{20}$H$_{28}$N$_{2}$O$_{5}$S.HCl

Relative molecular mass: 445.02

Chirality: $(R)$-(-) enantiomer

Solubility: Slightly soluble in water, sparingly soluble in ethanol and methanol, insoluble in non-polar organic solvents (hexane)
Optical rotation: The angle of optical rotation is between -3.0° and -4.5° (calculated with reference to the anhydrous substance)

Isomerism/polymorphism: Not described in literature

The quality of the drug substance is suitably controlled in line with the current edition of the Ph. Eur. monograph.

Synthesis of the drug substance from the designated starting material has been adequately described and appropriate in-process controls and intermediate specifications are applied. Satisfactory specification tests are in place for all starting materials and reagents, and these are supported by relevant Certificates of Analysis.

An appropriate specification is provided for the drug substance. Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications.

Appropriate proof-of-structure data have been supplied for the drug substance. All potential known impurities have been identified and characterised. Satisfactory Certificates of Analysis for all working standards have been provided. Batch analysis data are provided and comply with the proposed specification.

Satisfactory specifications and Certificates of Analysis have been provided for all packaging used to store the drug substance. Confirmation has been provided that the primary packaging complies with current guidelines concerning materials in contact with foodstuffs.

Appropriate stability data have been generated, supporting a suitable retest period when the drug substance is stored in the proposed packaging.

**Drug product**

Each film-coated prolonged-release tablet contains 400 micrograms tamsulosin hydrochloride and the excipients cellulose microcrystalline, hydroxypropylcellulose, lactose monohydrate, polyethylene oxide, butylhydroxytoluene, magnesium stearate, silica colloidal anhydrous, hypromellose, macrogol 400, titanium dioxide (E 171), talc, quinoline yellow (E 104), carmine (E 120) and iron oxide, black (E 172).

All excipients comply with their respective Ph. Eur. or NF monographs, with the exception of quinoline yellow (E 104), carmine (E 120) and iron oxide, black (E 172), which are controlled to in-house specifications. In the absence of relevant monographs for these excipients, this is acceptable. Satisfactory Certificates of Analysis have been provided for all excipients.

The only excipient of animal origin in the product is lactose. A statement is provided by the supplier of lactose confirming that it is in compliance with the requirements of the relevant guideline and Directives with regard to TSE.

**Pharmaceutical development**
The objective of the development programme was to develop a formulation similar to the innovator product, Flomax MR, 400 micrograms, prolonged release tablets (PL 00166/0171). A satisfactory account of the pharmaceutical development has been provided.

Comparative in vitro dissolution and impurity profiles have been provided for the proposed and reference products.

Manufacturing process
A satisfactory batch formula has been provided, along with an appropriate account of the manufacturing process. The manufacturing process has been validated and has shown satisfactory results.

Finished product specification
The finished product specification is acceptable. Test methods have been described and have been adequately validated. Batch data have been provided and comply with the release specifications. Certificates of Analysis have been provided for all working standards used.

Container closure system
The finished products are stored in aluminium/aluminium blister packs. Pack sizes vary for the different Marketing Authorisations and are as follows:

UK/H/2481/001/DC: 10, 14, 20, 28, 30, 50, 56, 60, 80, 90, 100 and 200
UK/H/2482/001/DC: 14, 20, 28, 30, 49, 50, 56, 98 and 100
UK/H/2483/001/DC: 10, 14, 20, 28, 30, 50, 56, 60, 80, 90, 100 and 200
UK/H/4466/001/DC: 10, 14, 20, 28, 30, 49, 50, 56, 60, 80, 90, 98, 100 and 200
UK/H/4467/001/DC: 10, 14, 20, 28, 30, 49, 50, 56, 60, 80, 90, 98, 100 and 200

Satisfactory specifications and Certificates of Analysis have been provided for all packaging components. All primary packaging complies with the current European regulations concerning materials in contact with foodstuffs.

Stability of the product
Stability studies were performed in accordance with current guidelines on the finished products in the packaging proposed for marketing. The data from these studies support a shelf-life of 2 years when the storage precaution ‘Store in the original package’ is applied.

Product literature
The SmPCs, PILs and product labels are pharmaceutically acceptable.

A package leaflet has been submitted to the MHRA along with results of consultations with target patient groups ("user testing"), in accordance with Article 59 of Council Directive 2001/83/EC, as amended. The results indicate that the package leaflet is well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that it contains.

Expert report
The pharmaceutical expert report has been written by an appropriately qualified person and is a suitable summary of the pharmaceutical dossier.

**Quality conclusion**
There are no objections to the approval of the Marketing Authorisation applications for Faramsil 400 microgram Prolonged-release Tablets and Tamsulosin 400 microgram Prolonged-release Tablets from a quality point of view.

**Preclinical aspects**

**Preclinical overview**
The pharmacological, pharmacokinetic and toxicological properties of tamsulosin are well known. As tamsulosin is a widely used, well known drug substance, no further studies are required and the applicant has provided none. An overview based on the literature is thus appropriate.

The preclinical overview has been written by an appropriately qualified expert. The overview, dated May 2008, refers to 37 references from the published literature dated up to 2007. In view of the fact that the pharmaco-toxicological properties of tamsulosin are well known, the overview is acceptable.

**Environmental risk assessment**
A suitable justification for the absence of a formal environmental risk assessment has been provided, based on the expectation that introduction of these generic products onto the market is unlikely to result in an increase in the combined sales of all tamsulosin-containing products, which in turn is unlikely to increase exposure of the environment to tamsulosin.

**Product literature**
The product literature is acceptable from a preclinical point of view.

**Preclinical conclusion**
There are no objections to the approval the Marketing Authorisation applications for Faramsil 400 microgram Prolonged-release Tablets and Tamsulosin 400 microgram Prolonged-release Tablets from a preclinical point of view.

**Clinical aspects**

**Pharmacokinetics**
To support the applications, three open label, single dose, randomised evaluations of the relative bioavailability of two formulations of tamsulosin 400 microgram prolonged release tablets in healthy adult human male subjects were carried out. In the first study the subjects were in a fasting state, in the second study they were in a fed state and the third study was a steady-state study.

**Methods used in all three studies**
The following products were used in the studies:
Test product: Tamsulosin Tablets 400 ug
Reference product: Alna Ocas 0.4 mg Retardtabletten (tamsulosin hydrochloride)

Subjects were admitted to the clinical facility at least 10 hours prior to study drug administration and remained in the clinical trial site until 24 hours post-dosing. They were provided a meal at least 10 hours prior to dosing.

There was a washout period of 14 days between the two periods of each study and this was sufficient to avoid carryover, as evidenced by tamsulosin being undetectable in the pre-dose samples in period two of all three studies.

Bioequivalence was to be concluded if the 90% Confidence Intervals for the ratios of the means of Ln-transformed pharmacokinetic parameters AUC₀-∞ and AUC₀-t for the test and reference formulations were within the bioequivalence limits of 80%-125%. For Cₘₐₓ the 90% Confidence Intervals were widened to 75-133%, due to the high intra-individual variability of tamsulosin.

Tamsulosin was measured using a validated LC-MS-MS method.

The pharmacokinetic parameters (Tₘₐₓ, Cₘₐₓ, AUC₀-t, AUC₀-∞, lambda z, kel and t₁/₂) were calculated from the plasma tamsulosin concentrations by non-compartmental analysis. The 90% Confidence Intervals for the ratios of the means of Ln-transformed pharmacokinetic parameters Cₘₐₓ and AUC₀-t were also calculated.

1. Fasting study

This was a four-period, two-treatment crossover trial, designed to demonstrate both bioequivalence between the test and reference products and the high pharmacokinetic variability of the reference product.

Method

Healthy male volunteers with an age range from 18 to 55 years were entered in the study.

A single oral dose (400 ug) of the assigned formulation was administered to subjects in a fasting state.

Serial blood samples were collected in each period. Tₘₐₓ for tamsulosin is around 6 hours in the fasting state and sampling frequency was sufficient for accurate Cₘₐₓ estimation.

Results

Bioequivalence results for Ln-transformed test/reference ratios with 90% Confidence Intervals:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Lower limit</th>
<th>Ratio</th>
<th>Upper limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUCₜ</td>
<td>102.80</td>
<td>110.520</td>
<td>118.14</td>
</tr>
<tr>
<td>AUCᵢ</td>
<td>104.68</td>
<td>113.06</td>
<td>122.11</td>
</tr>
<tr>
<td>Cₘₐₓ</td>
<td>114.87</td>
<td>121.48</td>
<td>128.46</td>
</tr>
</tbody>
</table>

Results of statistical analysis
The intra-subject CV of the reference product is more than 30%. According to the Guideline on the Investigation of Bioequivalence, as this is more than 30%, scaled average bioequivalence can be used.

Using the scaling approach, the criteria for the 90 % Confidence Interval for C_{max} is 77.04-129.79 %. The 90 % Confidence Interval for C_{max} given in the table above (114.87-128.46) is, therefore, within the required Confidence Interval.

**Conclusion**

The trial design is acceptable to assess both the bioequivalence and the potential highly variable nature of the product. As the applicant has sampled up to 72 hours, there are no concerns regarding the extrapolation of AUC_{t} to AUC_{inf}. The point estimate of variability is reliably estimated as being above 30%.

Both high variability and bioequivalence have been demonstrated. Therefore, it can be robustly concluded that the test and reference products, after a single dose (400 ug) administration, are bioequivalent.

**2. Fed study**

This was a two-treatment, two-period, crossover trial, designed to demonstrate bioequivalence between the test and reference products.

**Method**

Healthy male volunteers with an age range from 18 to 55 years were entered in the study.

A single oral dose (400ug) of the assigned formulation was administered to subjects in the fed state.

Serial blood samples were collected in each period. T_{max} for tamsulosin is around 6 hours in the fasting state and sampling frequency was sufficient for accurate C_{max} estimation.

**Results**

Bioequivalence results for Ln-transformed test/reference ratios with 90% Confidence Intervals:

<table>
<thead>
<tr>
<th>Tamsulosin</th>
<th>Parameters</th>
<th>Test</th>
<th>Reference</th>
<th>T/R ratio (%)</th>
<th>90% CI (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C_{max} (ng/mL)</td>
<td>9.10</td>
<td>9.08</td>
<td>101.67</td>
<td>91.97-112.40</td>
<td></td>
</tr>
<tr>
<td>AUC_{t} (ng.h/mL)</td>
<td>142.71</td>
<td>151.18</td>
<td>95.15</td>
<td>88.58-102.21</td>
<td></td>
</tr>
<tr>
<td>AUC_{∞} (ng.h/mL)</td>
<td>154.44</td>
<td>163.68</td>
<td>94.96</td>
<td>88.66-101.69</td>
<td></td>
</tr>
</tbody>
</table>

The applicant has concluded that the test and reference products are bioequivalent.
Conclusion
The trial design is acceptable to assess bioequivalence. Study drug was administered after a supervised breakfast. Subject withdrawals and other protocol deviations were managed satisfactorily. None of the pre-dose samples contained detectable level of tamsulosin, length of the washout period was adequate. Blood collection time up to 72 hours post-dose was sufficient.

Analytical methods were satisfactory. The methods of statistical analysis used were appropriate. The 90% confidence intervals for the ln-transformed AUC and C\text{max} lie within the acceptance criteria of 80-125%.

Based on the submitted bioequivalence study, the test and reference products, after a single dose (400 ug) administration, are bioequivalent.

3. Steady-state study
This was a two-treatment, two-period, crossover trial, designed to demonstrate bioequivalence between the test and reference products.

Method
Healthy male volunteers with an age range from 18 to 55 years were entered in the study.

A single oral dose (400ug) of the assigned formulation was administered to each subject on days 1-7.

T\text{max} for tamsulosin is around 6 hrs in the fasting state and sampling frequency was sufficient for accurate C\text{max} estimation.

Results
Bioequivalence results for Ln-transformed test/reference ratios with 90% Confidence Intervals:

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Test</th>
<th>Reference</th>
<th>T/R ratio (%)</th>
<th>90% CI (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C\text{min} (ng/mL)</td>
<td>2.62</td>
<td>2.49</td>
<td>105.07</td>
<td>89.88-122.82</td>
</tr>
<tr>
<td>C\text{max} (ng/mL)</td>
<td>7.94</td>
<td>7.67</td>
<td>102.99</td>
<td>91.19-116.31</td>
</tr>
<tr>
<td>AUC\text{t} (ng,h/mL)</td>
<td>106.82</td>
<td>101.18</td>
<td>105.17</td>
<td>93.06-118.85</td>
</tr>
</tbody>
</table>

The applicant has concluded that the test and reference products are bioequivalent.

Conclusion
The two-period, two-sequence cross-over study design is appropriate. Study drug was administered daily (days 1-7) to achieve a steady state. Subject withdrawals and other protocol deviations were managed satisfactorily. None of the pre-dose samples contained detectable level of tamsulosin, length of the washout period was adequate. Blood collection time up to 72 hours post-dose was sufficient.
Analytical methods were satisfactory. The methods of statistical analysis used were appropriate. The 90% confidence intervals for the ln-transformed AUC and $C_{max}$ lie within the acceptance criteria of 80-125%.

Based on the submitted bioequivalence study, the test and reference products, in the steady state, are bioequivalent.

**Pharmacodynamics**
The pharmacodynamic characteristics of tamsulosin have been well-studied in the past. There would be no particular concerns for a generic medicinal product. No new data have been submitted and none are required.

**Clinical efficacy and safety**
No new efficacy data are presented and none is required. A comprehensive review of the published literature has been provided by the applicant, citing the well established clinical pharmacology, efficacy and safety of tamsulosin.

**Pharmacovigilance system**
The RMS considers that the pharmacovigilance system fulfils the requirements. The applicant has the services of a qualified person responsible for pharmacovigilance and has the necessary means for the collection and notification of any adverse reaction suspected of occurring in the Community or in a third country.

**Risk management plan**
No safety concerns requiring additional risk minimization activities have been identified. A detailed RMP is not considered necessary for these applications.

**Expert report**
The clinical overview has been written by an appropriately qualified physician. The overview, dated July 2008, refers to 150 references from the published literature dated up to 2007 and is acceptable.

**Product literature**
All product literature (SmPC, PIL and labelling) is medically satisfactory.

**Clinical conclusion**
There are no objections to the approval the Marketing Authorisation applications for Faramsil 400 microgram Prolonged-release Tablets and Tamsulosin 400 microgram Prolonged-release Tablets from a clinical point of view.
OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

QUALITY
The important quality characteristics of Faramsil 400 microgram Prolonged-release Tablets and Tamsulosin 400 microgram Prolonged-release Tablets are well-defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit-risk balance.

PRECLINICAL
No new preclinical data were submitted and none are required for applications of this type.

EFFICACY
The use of tamsulosin in the treatment of lower urinary tract symptoms associated with benign prostatic hyperplasia is well established. Bioequivalence has been demonstrated between the proposed products and their reference product. New efficacy data is, therefore, not needed.

SAFETY
No new or unexpected safety concerns arise from these applications.

The SmPCs and PILs are satisfactory and consistent with that of the reference product. Satisfactory labelling has also been submitted.

BENEFIT-RISK ASSESSMENT
The quality of the products is acceptable and no new preclinical or clinical safety concerns have been identified. Extensive clinical experience with tamsulosin is considered to have demonstrated the therapeutic value of the compound. The benefit-risk ratio is, therefore, considered to be acceptable. Marketing Authorisations should be granted.