SUMMARY OF THE PRODUCT CHARACTERISTICS

1. Name of Medicinal Product

Tamcontin 0.4
(Controlled Release Tablets of Tamsulosin Hydrochloride)

2. Qualitative and Quantitative Composition

Core

Name of ingredients	Unit formula (mg/tablet)	Active/ Non-active	Reference to standard	Reason for inclusion
Tamsulosin Hydrochloride	0.412*	Active	In-house	Alpha-adrenoreceptor antagonists
Cetostearyl Alcohol (Kolliwax CSA 50)	10.00	Non-Active	BP	Release Retardant
Lactose	60.00	Non-Active	BP	Diluent
Povidone K-30	4.00	Non-Active	USP	Binder
Magnesium Stearate	1.00	Non-Active	BP	Lubricant
Microcrystalline Cellulose	31.588	Non-Active	BP	Diluent
Hydroxyethylcellulose (Natrosol 250 HX)	10.00	Non-Active	BP	Release Retardant
Purified Talc	1.00	Non-Active	BP	Glident
Purified Water	64.0**	Non-Active	BP	Solvent

* Contain 3% Overage
** Not present in final weight

Coating

Name of ingredients	Unit formula (mg / tablet)	Active / Non-active	Reference to standard	Reason for inclusion
Acryl-Eze 93 O 18359 White	10.00	Non-Active	In-house	Acid protective coating material
Purified Water	56.75***	Non-Active	BP	Solvent

***Not present in final weight

3. Pharmaceutical Form

Controlled Release Tablets

4. Clinical Particulars

4.1 Therapeutic Indications

For the treatment of symptoms of benign prostatic hyperplasia (BPH). Not indicated for the treatment of hypertension.

4.2 Posology and Method of Administration

Dosage of 0.4 mg once daily is recommended for the treatment of signs and symptoms of benign prostatic hyperplasia (BPH). The tablet is to be swallowed whole and not crushed or chewed. It should be administered approximately at half an hour following the same meal each day.
For those patients who fail to respond to the 0.4 mg dose after two to four weeks of dosing, the dose of tamsulosin tablets can be increased to 0.8 mg once daily. If therapy is discontinued or interrupted for several days at either the 0.4 mg or 0.8 mg dose, therapy should be started again with the 0.4 mg once daily dose.

4.3 Contraindications

Hypersensitivity to tamsulosin hydrochloride or any other component of the formulation. History of orthostatic hypotension and severe hepatic insufficiency.

4.4 Special warnings and special precautions for use

As with other alpha-1 blockers, a reduction in blood pressure can occur during treatment as a result of which, rarely, syncope may occur. At the first signs of orthostatic hypotension such as dizziness or weakness, the patient should sit or lie down until the symptoms have disappeared.

Patients should be evaluated prior to the start of the therapy to rule out the presence of carcinoma of the prostate. Digital rectal examination and when necessary determination of prostate specific antigen (PSA) should be performed before treatment and at regular intervals afterwards.

Very rarely, like with other alpha adrenoreceptor antagonists, priapism can occur. Because this condition can lead to permanent impotence if not properly treated, patients must be advised about the seriousness of the condition.

The treatment of patients with severe renal impairment (creatinine clearance of less than 10ml/min) should be done with caution as studies with such patients have not been done.

Intraoperative Floppy Iris Syndrome (IFIS): IFIS, a variant of small pupil syndrome, has been observed during cataract surgery in some patient treated with alpha-1 blocker. Most reports were in patients taking the alpha-1 blocker when IFIS occurred, but in some cases, the alpha-1-blocker had been stopped prior to surgery (2 to 14 days). In a few cases, IFIS was reported after the patient had been off the alpha-1 blocker for a longer period (5 weeks to 9 months).

The patient's ophthalmologist should be prepared for possible modification to their surgical technique such as the utilization of iris hooks, iris dilator rings or viscoelastic substances. The benefit of stopping alpha -1 blocker therapy prior to cataract surgery has not been established.

Sulfa allergy: In patients with sulfa allergy, allergic reaction to tamsulosin hydrochloride has been rarely reported. If a patient reports a serious or life threatening sulfa allergy, caution is warranted when administering tamsulosin hydrochloride.

Children:
Not indicated for use in paediatric population.

4.5 Interaction with other medicinal products and other forms of Interaction.

Though there are no studies on the pharmacokinetic or the pharmacodynamic interactions between tamsulosin and other adrenergic blocking agents, there is a theoretical risk of enhanced hypotensive effect when given concurrently with drugs which may reduce blood pressure, including anaesthetic agents and other alpha-1 adrenoreceptor antagonists.

Concurrent administration with sildenafil, tadalafil and vardenafil may also increase the risk of a drop in blood pressure. Doses of sildenafil greater than 25 mg should be taken at least four hours apart from taking tamsulosin.

Concomitant cimetidine causes a rise in the plasma levels and a decrease in the clearance of tamsulosin, therefore caution is advised, particularly at doses higher than 0.4mg. Frusemide leads to a fall in the plasma levels of tamsulosin.

No interactions were observed when tamsulosin was given concomitantly with atenolol, enalapril, nifedipine, digoxin or theophylline.

In vitro studies show that diazepam, propranolol, trichlormethiazide, chlormadinon, amitriptyline, diclofenac, glibenclamide, warfarin and simvastatin do not change the free fraction of tamsulosin in the human plasma and vice versa. No interactions at the level of hepatic metabolism have been seen during in vitro studies with liver microsomal fractions involving salbutamol, glibenclamide, amitriptyline and finasteride. Diclofenac and warfarin may however increase the elimination rate of tamsulosin.

4.6 Pregnancy and Lactation

Not applicable as tamsulosin is intended for male patients only.
Ejaculation disorders have been observed in short- and long-term clinical studies with tamsulosin. Events of ejaculation disorder, retrograde ejaculation and ejaculation failure have been reported in the post authorisation phase.

4.7 Effects on ability to drive and use machines

No data is available on whether Tamcontin 0.4 tablets adversely affect the ability to drive or operate machines. However, in this respect patients should be aware of the fact that drowsiness, blurred vision, dizziness and syncope can occur.

4.8 Undesirable Effects

The following adverse reactions have been reported during the use of tamsulosin: dizziness, abnormal ejaculation and, less frequently (1-2%) headache, asthenia, postural hypotension, palpitations and rhinitis.
Gastrointestinal reactions such as nausea, vomiting, diarrhea, and constipation occasionally occur. Hypersensitivity reactions such as rash, pruritus, and urticaria can occur occasionally. As with other alpha-blockers, drowsiness, blurred vision, dry mouth or oedema can occur. Syncope has been reported rarely, and there have been very rare reports of angioedema and priapism.

4.9 Overdose

Overdosage with tamsulosin hydrochloride can potentially result in severe hypotensive effects, dizziness and malaise. Severe hypotensive effects have been observed at different levels of overdosing
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 does not help, then volume expanders, and when necessary, vasopressors could be employed. Renal function should be monitored and general supportive measures applied. Dialysis is unlikely to be of help, as tamsulosin is very highly bound to plasma proteins.

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

5. Pharmacological Properties

Mechanism of action
Tamsulosin binds selectively and competitively to postsynaptic alpha$_1$-receptors, in particular to the subtype alpha$_{1A}$, which bring about relaxation of the smooth muscle of the prostate, whereby tension is reduced.

5.1 Pharmacodynamic Properties

Flomaxtra XL 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. Alpha$_1$-blockers can reduce blood pressure by lowering peripheral resistance. No reduction in blood pressure of any clinical significance was observed during studies with Flomaxtra XL.

Paediatric Population

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

5.2 Pharmacokinetic Properties

The pharmacokinetics of tamsulosin hydrochloride have been evaluated in adult healthy volunteers and patients with BPH after single and/or multiple administration with doses ranging from 0.1 mg to 1 mg. Absorption of tamsulosin is essentially complete following oral administration under fasting conditions (>90%). It exhibits linear kinetics following single or multiple dosing, with achievement of steady state concentrations on the fifth day of once a day dosing.
Tamsulosin is 99% bound to plasma proteins. The time to reach maximum concentration is four to five hours under fasting conditions and six to seven hours when it is administered with food. Absorption is reduced by a recent meal before the dose but the uniformity of absorption can be promoted by taking the drug after the same meal everyday. Tamsulosin is extensively metabolized by the cytochrome P450 enzymes in the liver and less than 10% of the dose is excreted in the urine unchanged. On administration of the radiolabelled dose of tamulosin to four healthy volunteers, 97% of the administered radioactive substance was recovered, with urine

(76%) representing the primary route of excretion compared to faeces (21%) over 168 hours. Following intravenous or oral administration of an immediate release formulation, the elimination half life of tamsulosin in plasma ranges from 5 to 7 hours. Because of the absorption rate controlled pharmacokinetics with controlled release tamsulosin tablets, the apparent half life of tamsulosin is approximately 9 to 13 hours in healthy volunteers and 14 to 15 hours in the target population.
Pharmacokinetic studies indicate that disposition of tamsulosin may be slightly prolonged in geriatric males as compared to young healthy male volunteers. Therefore, greater sensitivity of some older individuals cannot be ruled out. Patients with mild to moderate renal and hepatic impairment do not require any dosage adjustment but those with end stage renal disease have not been studied.

5.3 Preclinical safety data

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

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

6. Pharmaceutical Particulars

6.1 List of Excipients

Excipients
Cetostearyl Alcohol (Kolliwax CSA 50)
Lactose
Povidone K-30
Magnesium Stearate
Microcrystalline Cellulose
Hydroxyethylcellulose (Natrosol 250 HX)
Purified Talc
Purified Water
Acryl-Eze 93 O 18359 White

6.2 Incompatibilities

None of the incompatibilities has been reported.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at or below 30^{o} C, in a dry place, protected from light.
Keep out of reach of children.

6.5 Nature and content of container

Primary Packaging
Tamcontin 0.4 are packed in an aluminium strip made up of printed aluminium foil (width 131 mm × thickness 0.04 mm) and plain aluminium foil (width 131 mm × thickness 0.04 mm).

Secondary Packaging
The Aluminium strip of 10s is packaged in an outer carton printed in approved colour and design and contain a package insert comprising of Cream wove art paper.

6.6 Special precautions for disposal and other handling

No special requirements.

Pack Size
Box of 100 tablets (10x10's strips)
Box of 30 tablets (3x10's strips)

6.6 Instructions for use/handling

Keep out of reach of children,

The tablets should be swallowed whole and not chewed.

7. Marketing authorization holder

Modi-Mundipharma Private Limited
1400, Modi Tower, 98 Nehru Place,
New Delhi – 110019,
India

PHILLIPS PHARMACEUTICALS (NIGERIA) LIMITED,
122-132 AFPRINT INDUSTRIAL ESTATE APAPA-OSHODI EXPRESSWAY IYANA-ISOLO LAGOS
NIGERIA 8035493198
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8.0 Marketing authorization number

A4-101181

9.0 Date of first authorization/renewal of the authorization

30/01/2025

10.0 Date of (partial) revision of the text

19/10/2021