SUMMARY OF PRODUCT CHARACTERISTICS

CONTIFLO OD CAPSULES

(Tamsulosin Hydrochloride Extended Release Capsules 0.4 mg)

1. NAME OF THE MEDICINAL PRODUCT

CONTIFLO OD CAPSULES

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

COMPOSITION

CONTIFLO OD CAPSULES 0.4 mg
Each capsule contains
Tamsulosin hydrochloride…… 0.4 mg.

For list of excipients please see **Section 6.1**

3. PHARMACEUTICAL FORM

Extended Release Capsule.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of functional symptoms of benign prostatic hyperplasia (BPH).

4.2 Posology and method of administration

Male 45 to 75 years.

One capsule daily, to be taken after the same meal each day.

The capsule should be swallowed whole and should not be crunched or chewed as this will interfere with the modified release of the active ingredient.

4.3 Contraindications

Hypersensitivity to tamsulosin hydrochloride, including drug induced angioedema, or any other component of the product; 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, as a result of which, rarely, syncope can occur. At the first signs of orthostatic hypotension (dizziness, weakness) the patient should sit or lie down until the symptoms have disappeared.

The 'Intraoperative Floppy Iris Syndrome' (IFIS, a variant of small pupil syndrome) has been observed during cataract and glaucoma surgery in some patients on or previously treated with tamsulosin hydrochloride. IFIS may increase the risk of eye complications during and after the operation.

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

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

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

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

Additional warnings when supplied as a non-prescription medicine

Tamsulosin should not be given to patients receiving antihypertensive medicines with significant alpha1 adrenoceptor antagonist activity (e.g. doxazosin, indoramin, prazosin, terazosin, verapamil) without first consulting a doctor.

Tamsulosin should not be given to a man who experiences postural hypotension.

Tamsulosin should not be supplied to any man with heart, renal, or liver disease, uncontrolled diabetes, urinary incontinence, or to a man who has had prostate surgery.

Tamsulosin should not be supplied to a man whose symptoms are of less than 3 months duration.

Tamsulosin should not be given to any man who reports dysuria, haematuria, or cloudy urine, in the past 3 months, or who is suffering from a fever that might be related to a urinary tract infection.

Tamsulosin should not be used in those planning to have eye surgery for cataract or glaucoma, or who have recently experienced blurred or cloudy vision that has not been examined by a doctor or optician.

If urinary symptoms have not improved within 14 days of starting treatment with tamsulosin, or are getting worse, the patient should stop taking tamsulosin and be referred to the doctor.

Medical review is required for the diagnosis of BPH. Patients must see their doctor within 6 weeks of starting treatment, for assessment of their symptoms and confirmation that they can continue to take tamsulosin.

Every 12 months, patients should be advised to consult a doctor for a clinical review.

4.5 Interaction with other medicinal products and other forms of interaction

Interaction studies have only been reported in adults.

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

In vitro neither diazepam nor propranolol, trichlormethiazide, chlormadinon, 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.

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

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

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

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

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

There is a theoretical risk of enhanced hypotensive effect when given concurrently with drugs which may reduce blood pressure including anaesthetic agents, other alpha1adrenoceptor antagonists.

4.6 Pregnancy and lactation

Tamsulosin is not indicated for use in women.

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

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

System Organ Class	Common (>1/100, <1/10)	Uncommon (>1/1 000, <1/100)	Rare (>1/10 000, <1/1 000)	Very rare (<1/10 000)	Not Known (cannot be estimated from the available data)
Nervous system disorders	dizziness	headache	syncope		
Eye disorders					Vision blurred* Visual impairment*
Cardiac disorders		palpitations			
Vascular disorders		orthostatic hypotension			
Respiratory, thoracic and mediastinal disorders		rhinitis			Epistaxis*
Gastro-intestinal disorders		constipation, diarrhoea, nausea, vomiting			Dry Mouth*
Skin and subcutaneous tissue disorders		rash, pruritus, urticaria	angioedema	Stevens-Johnson syndrome	Erythema multiforme* Dermatitis exfoliative*
Reproductive systems and breast disorders	ejaculation disorders, including retrograde ejaculation and ejaculation failure			priapism	
General disorders and		asthenia			

administration site disorders					

*reported during post-marketing.

As with other alpha-blockers, drowsiness or oedema can occur.

During cataract and glaucoma surgery a small pupil situation, known as Intraoperative Floppy Iris Syndrome (IFIS), has been reported with therapy of tamsulosin during post-marketing surveillance (see **Section 4.4**).

Post-marketing experience: In addition to the adverse events listed above, atrial fibrillation, arrhythmia, tachycardia and dyspnoea have been reported in association with tamsulosin use. Because these spontaneously reported events are from the worldwide post-marketing experience, the frequency of events and the role of tamsulosin in their causation cannot be estimated from the reported data.

4.9 Overdose

Symptoms: Overdosage with tamsulosin hydrochloride can potentially result in severe hypotensive effects. Severe hypotensive effects have been reported at different levels of overdosing.

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

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

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group:
Alpha$_1$-adrenoceptor antagonist.

Preparations for the exclusive treatment of prostatic disease.

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

Pharmacodynamic effects:
Tamsulosin hydrochloride increases maximum urinary flow rate by reducing smooth muscle tension in prostate and urethra and thereby relieving obstruction.

It also improves the complex of irritative and obstructive symptoms in which bladder instability and tension of the smooth muscles of the lower urinary tract play an important role. Alpha$_1$-blockers can reduce blood pressure by lowering peripheral resistance. No reduction in blood pressure of any clinical significance was reported during studies with tamsulosin.

5.2 Pharmacokinetics properties

Absorption
Tamsulosin hydrochloride is absorbed from the intestine and is almost completely bioavailable.
Absorption of tamsulosin hydrochloride is reduced by a recent meal. Uniformity of absorption can be promoted by the patient always taking tamsulosin after the same meal each day. Tamsulosin shows linear kinetics.

After a single dose of tamsulosin in the fed state, plasma levels of tamsulosin has been reported to peak at around 6 hours and, in the steady state, which is reached by day 5 of multiple dosing, C_{max} in patients is about two thirds higher than that reached after a single dose. Although this was reported in elderly patients, the same finding would also be expected in young ones. A considerable inter-patient variation in plasma levels has been reported, both after single and multiple dosing.

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

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

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

The reported *in vitro* results suggest that CYP3A4 and also CYP2D6 are involved in metabolism, with possible minor contributions to tamsulosin hydrochloride metabolism by other CYP isozymes. Inhibition of CYP3A4 and CYP2D6 drug metabolising enzymes may lead to increased exposure to tamsulosin hydrochloride (see **Section 4.4; 4.5**). No dose adjustment is warranted in hepatic insufficiency. None of the metabolites are more active than the original compound.

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

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

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

5.3 Preclinical safety data

Carcinogenesis, mutagenesis, impairment of fertility

Single and repeat dose toxicity studies were reported in mice, rats and dogs. In addition reproduction toxicity studies were reported 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 reported to be altered in dogs. This response is considered to be not clinically relevant. Tamsulosin reported 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 reported at high dose levels are regarded as irrelevant.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline cellulose (PH 101), magnesium stearate, methacrylic acid-ethyl acrylate copolymer (1:1) dispersion (30%), purified water, sodium hydroxide, triacetin, purified talc, titanium dioxide

6.2 Incompatibilities

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store below 30^{o}C, protected from moisture.

6.5 Nature and contents of container

PVC/PVDC Blister pack of 10's and 30's.

6.6 Special precautions for disposal and other handling

Keep all medicines out of the reach of children.

7. MARKETING AUTHORISATION HOLDER

Ranbaxy Nigeria Limited

8. MARKETING AUTHORISATION NUMBER(S)

04-9467

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

03-Nov-2006

10. DATE OF REVISION OF THE TEXT

Jan 2018

REFERENCES

1. Summary of Product Characteristics of **Flomax Relief MR®** film coated tablets, Boehringer Ingelheim Limited, UK, revised in April 2014.