Summary of Product Characteristics

1. Name of the medicinal product
Floezy (Tamsulosin Hydrochloride) 0.4 mg prolonged-release hard capsules

2. Qualitative and quantitative composition
Each capsule contains tamsulosin hydrochloride at an amount of 0.4 mg, which equals to tamsulosin 0.367 mg.
For the full list of excipients, see section 6.1.

3. Pharmaceutical form
White, un-scored, round tablets with a diameter of 9 mm debossed on one side with "T9SL" and "0.4" on the other side.

4. Clinical particulars
4.1 Therapeutic indications

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

4.2 Posology and method of administration

Posology
One capsule daily after breakfast or after the first daily meal.
Hepatic/renal impairment
No dose adjustment is warranted in renal impairment.
No dose adjustment is warranted in patients with mild to moderate hepatic insufficiency (see section 4.3).
Paediatric population
The safety and efficacy of tamsulosin hydrochloride in children < 18 years have not been established. Currently available data are described in section 5.1.
Method of administration
Oral use.
The capsule is swallowed whole, without crushing or chewing, because otherwise the controlled release of the active ingredient would be affected.

4.3 Contraindications

• Hypersensitivity to the active substance including drug-induced angioedema or to any of the excipients listed in section 6.1.
• History of orthostatic hypotension.
• Severe hepatic insufficiency.
• Micturition syncope history

4.4 Special warnings and precautions for use

As with other α_1-adrenoceptors antagonists, a reduction in blood pressure can occur in individual cases during treatment with tamsulosin hydrochloride as a result of which, rarely, syncope can occur. At the first signs of orthostatic hypotension (dizziness, weakness), the patient should sit or lie down until the symptoms have disappeared.

Before therapy with tamsulosin hydrochloride is initiated, the patient should be examined in order to exclude the presence of other conditions, which can cause the same symptoms as benign

prostatic hyperplasia. Digital rectal examination and, when necessary, determination of prostate specific antigen (PSA) should be performed before treatment and at regular intervals afterwards. The treatment of patients with severe renal impairment (creatinine clearance of < 10 ml/min) should be approached with caution, as these patients have not been studied.

Angioedema has been rarely reported after the use of tamsulosin. In case of angioedema, treatment should be discontinued immediately, the patient should be monitored until disappearance of the oedema, and tamsulosin should not be re-administered.

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 yet been established. IFIS has also been reported in patients who had discontinued tamsulosin for a longer period prior to the surgery.

The initiation of therapy with tamsulosin hydrochloride in patients for whom cataract or glaucoma surgery is scheduled is not recommended. During pre-operative 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 in patients with poor metaboliser CYP2D6 phenotype.

Tamsulosin hydrochloride should be used with caution in combination with strong and moderate inhibitors of CYP3A4 (see section 4.5).
Excipient
This medicine contains less than 1 mmol sodium (23 mg) per capsule, that is to say essentially 'sodium-free'.

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 hydrochloride was given concomitantly with either atenolol, enalapril or theophylline. Concomitant cimetidine brings about a rise in plasma levels of tamsulosin, whereas furosemide a fall, but as levels remain within the normal range posology need not be adjusted.

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.

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 C_{max} 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 in patients with poor metaboliser CYP2D6 phenotype.

Tamsulosin hydrochloride should be used with caution in combination with strong and moderate inhibitors of CYP3A4.

Concomitant administration of tamsulosin hydrochloride with paroxetine, a strong inhibitor of CYP2D6, resulted in a C_{max} 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.

Concurrent administration of other α_1-adrenoceptor antagonists could lead to hypotensive effects.

4.6 Fertility, pregnancy and lactation

Tamsulosin is not indicated for use in women.
Ejaculation disorders have been observed in short- and long-term clinical studies with tamsulosin. Events of ejaculation disorder, retrograde ejaculation and ejaculation failure have been reported in the post authorization phase.

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 dizziness can occur.

4.8 Undesirable effects

Tabulated list of adverse reactions
The frequency of adverse reactions of tamsulosin listed below is defined using the following convention: Common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to < 1/1,000); very rare (< 1/10,000), not known (cannot be estimated from the available data).

MedDRA system organ class	**Frequency**	**Adverse reaction**
Nervous system disorders	Common	Dizziness (1.3%)
	Uncommon	Headache
	Rare	Syncope
Eye disorders	Not known	Vision blurred*, visual impairment*
Cardiac disorders	Uncommon	Palpitations
Vascular disorders	Uncommon	Orthostatic hypotension
Respiratory, thoracic and mediastinal disorders	Uncommon	Rhinitis
	Not known	Epistaxis*
Gastrointestinal disorders	Uncommon	Constipation, diarrhoea, nausea, vomiting
	Not known	Dry mouth*
Skin and subcutaneous tissue disorders	Uncommon	Rash, pruritus, urticaria
	Rare	Angioedema
	Very rare	Stevens-Johnson syndrome

	Not known	Erythema multiforme*, dermatitis exfoliative*
Reproductive system and breast disorders	Common	Ejaculation disorder, retrograde ejaculation, ejaculation failure
	Very rare	Priapism
General disorders and administration site conditions	Uncommon	Asthenia

* Observed post-marketing.
During cataract and glaucoma 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 hydrochloride 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.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Health care providers are asked to report any suspected adverse reactions to the marketing authorisation holder, or, if available, via the national reporting system (see details below).

Paper based reporting: TMDA yellow card
Online reporting: https://sqrt.tmda.go.tz/
USSD reporting: send a simple short text message to report any suspected Adverse Drug Reaction by dialing *152*00# and follow the instructions.

4.9 Overdose

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

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

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

5. Pharmacological properties
5.1 Pharmacodynamic properties

Pharmacotherapeutic category: Urologicals: Drugs used in benign prostatic hypertrophy.

ATC code: G04CA02.
The product is designed exclusively for the treatment of diseases of the prostate.

Mechanism of action
Tamsulosin binds selectively and competitively to post-synaptic α_1-adrenoreceptors, prevailingly their subtypes designated α_{1A} and α_{1D}. Thus, relaxation of smooth muscles of the prostate and urethra is achieved, which leads to a reduction of tonus and an improvement of the urinary flow.

Pharmacodynamic effects
Tamsulosin increases the maximum urinary flow. Due to relaxation of smooth muscles in the prostate and the urethra, obstruction is decreased, which leads to alleviation of voiding symptoms. Tamsulosin also alleviates the storage symptoms in the development of which also the instability of the urinary bladder is involved at a significant extent. The effects on symptoms of filling and depletion of the urinary bladder persist during long-term treatment. The necessity of surgical treatment or catheterization is significantly delayed owing to these effects.

α_1-blockers can reduce blood pressure by lowering peripheral resistance. No reduction in blood pressure of any clinical significance was observed during studies with tamsulosin in normotensive patients.

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

5.2 Pharmacokinetic properties

Absorption
Tamsulosin is absorbed from the intestinal tract and its bioavailability is almost complete. The absorption of tamsulosin decreases if the product is administered shortly after the meal. The uniformity of absorption may be supported via using tamsulosin capsules always after the same daily meal.

Kinetics of tamsulosin is linear.

After a single dose of tamsulosin taken after a full meal, the peak plasma levels are achieved at approximately 6 hours. The steady state is reached by day five of multiple dosing, when C_{max} in patients is about two thirds higher than that reached after a single dose. Although this has been demonstrated only in the elderly, the same result would also be expected in younger patients.
There are huge inter-patient variations in plasma levels of tamsulosin, both after single as well as multiple dosing.

Distribution

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

Biotransformation
Tamsulosin has a low first pass metabolic effect. The majority of tamsulosin is present in plasma in an unchanged form. Tamsulosin is metabolized in the liver.
In studies on rats, an induction of microsomal liver enzymes induced by tamsulosin has not been practically observed.

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

Dosage adjustment is not necessary in mild hepatic insufficiency.

The metabolites are not as effective and toxic as the active medicinal product itself.

Elimination
Tamsulosin and its metabolites are mainly excreted in the urine; approximately 9% of the dose given is released in an unchanged form.

The elimination half-life of tamsulosin in patients is approximately 10 hours (when taken after a meal) and 13 hours in the steady state.

In case of renal affections, no reduction of tamsulosin doses is substantiated.

5.3 Preclinical safety data

Toxicity after a single dose and multiple dosing has been investigated in mice, rats and dogs. Reproductive toxicity has also been investigated in rats, carcinogenicity in mice and rats, and genotoxicity *in vivo* and *in vitro*. The common toxicity profile with large doses of tamsulosin is equivalent to the pharmacological effect associated with alpha adrenergic antagonists.

Changes in ECG readings were found with very large doses in dogs. This is not, however, assumed to be of any clinical significance. Tamsulosin has not been found to have any significant genotoxic properties.

An increased incidence of proliferative alterations in the mammary glands of rat and mice females has been found. These findings, which are probably indirectly linked to hyperprolactinaemia and only occur as a result of large doses having been taken, are considered clinically insignificant.

6. Pharmaceutical particulars
6.1 List of excipients

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Keep out of reach of children. Protect from light and moisture.
Store below 30ºC in a dry place.

6.5 Nature and contents of container

3X10 Alu/PVC blister pack.

6.6 Special precautions for disposal and other handling

No special requirements.

7. Marketing authorization holder

Mega Lifesciences Public Company Limited
Address - 384 Moo 4, Pattana 3 Road,
Bangpoo Industrial Estate,
Soi 6, Preaksa, Muang Samutprakarn,
Samutprakarn 10280, Thailand

8. Marketing authorization number(s)

TAN 20 HM 0147

9. Date of first authorization/renewal of the authorization

July 09, 2020

10. Date of revision of the text

October 16, 2023