ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

TOVIAZ 4 mg prolonged-release tablets
TOVIAZ 8 mg prolonged-release tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

TOVIAZ 4 mg tablets
Each prolonged-release tablet contains fesoterodine fumarate 4 mg corresponding to 3.1 mg of fesoterodine.

TOVIAZ 8 mg tablets
Each prolonged-release tablet contains fesoterodine fumarate 8 mg corresponding to 6.2 mg of fesoterodine.

Excipients with known effect

TOVIAZ 4 mg tablets
Each 4 mg prolonged-release tablet contains 0.525 mg of soya lecithin and 91.125 mg of lactose.

TOVIAZ 8 mg tablets
Each 8 mg prolonged-release tablet contains 0.525 mg of soya lecithin and 58.125 mg of lactose.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Prolonged-release tablet.

TOVIAZ 4 mg tablets
The 4 mg tablets are light blue, oval, biconvex, film-coated, and engraved on one side with the letters 'FS'.

TOVIAZ 8 mg tablets
The 8 mg tablets are blue, oval, biconvex, film-coated, and engraved on one side with the letters 'FT'.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

TOVIAZ is indicated in adults for treatment of the symptoms (increased urinary frequency and/or urgency and/or urgency incontinence) that may occur with overactive bladder syndrome.

4.2 Posology and method of administration

Posology

Adults (including elderly)
The recommended starting dose is 4 mg once daily. Based upon individual response, the dose may be increased to 8 mg once daily. The maximum daily dose is 8 mg.

Full treatment effect was observed between 2 and 8 weeks. Hence, it is recommended to re-evaluate the efficacy for the individual patient after 8 weeks of treatment.

In subjects with normal renal and hepatic function receiving concomitant administration of potent CYP3A4 inhibitors, the maximum daily dose of TOVIAZ should be 4 mg once daily (see section 4.5).

Special population

Renal and hepatic impairment
The following table provides the daily dosing recommendations for subjects with renal or hepatic impairment in the absence and presence of moderate and potent CYP3A4 inhibitors (see sections 4.3, 4.4, 4.5 and 5.2).

		Moderate[3] or potent[4] CYP3A4 inhibitors		
		None	Moderate	Potent
Renal impairment[1]	Mild	4→8 mg[2]	4 mg	Should be avoided
	Moderate	4→8 mg[2]	4 mg	Contraindicated
	Severe	4 mg	Should be avoided	Contraindicated
Hepatic impairment	Mild	4→8 mg[2]	4 mg	Should be avoided
	Moderate	4 mg	Should be avoided	Contraindicated

(1) Mild GFR = 50-80 ml/min; Moderate GFR = 30-50 ml/min; Severe GFR = <30 ml/min
(2) Cautious dose increase. See sections 4.4, 4.5 and 5.2
(3) Moderate CYP3A4 inhibitors. See section 4.5
(4) Potent CYP3A4 inhibitors. See sections 4.3, 4.4 and 4.5

TOVIAZ is contraindicated in subjects with severe hepatic impairment (see section 4.3).

Paediatric population
The safety and efficacy of TOVIAZ in children aged less than 6 years have not been established. No data are available.

The safety and efficacy of TOVIAZ in children aged 6 years to 17 years have not been established. Currently available data are described in sections 5.1 and 5.2 but no recommendation on a posology can be made.

Method of administration
Tablets are to be taken once daily with liquid and swallowed whole. TOVIAZ can be administered with or without food.

4.3 Contraindications

- Hypersensitivity to the active substance or to peanut or soya or to any of the excipients listed in section 6.1
- Urinary retention
- Gastric retention
- Uncontrolled narrow angle glaucoma
- Myasthenia gravis
- Severe hepatic impairment (Child Pugh C)
- Concomitant use of potent CYP3A4 inhibitors in subjects with moderate to severe hepatic or renal impairment
- Severe ulcerative colitis
- Toxic megacolon.

4.4 Special warnings and precautions for use

TOVIAZ should be used with caution in patients with:

- Clinically significant bladder outflow obstruction at risk of urinary retention (e.g. clinically significant prostate enlargement due to benign prostatic hyperplasia, see section 4.3)
- Gastrointestinal obstructive disorders (e.g. pyloric stenosis)
- Gastro-oesophageal reflux and/or who are concurrently taking medicinal products (such as oral bisphosphonates) that can cause or exacerbate oesophagitis
- Decreased gastrointestinal motility
- Autonomic neuropathy
- Controlled narrow-angle glaucoma

Caution should be exercised when prescribing or uptitrating fesoterodine to patients in whom an increased exposure to the active metabolite (see section 5.1) is expected:

- Hepatic impairment (see sections 4.2, 4.3 and 5.2)
- Renal impairment (see sections 4.2, 4.3 and 5.2)
- Concomitant administration of potent or moderate CYP3A4 inhibitors (see sections 4.2 and 4.5)
- Concomitant administration of a potent CYP2D6 inhibitor (see sections 4.5 and 5.2).

Dose increases
In patients with a combination of these factors, additional exposure increases are expected. Dose dependent antimuscarinic adverse reactions are likely to occur. In populations where the dose may be increased to 8 mg once daily, the dose increase should be preceded by an evaluation of the individual response and tolerability.

Organic causes must be excluded before any treatment with antimuscarinics is considered. Safety and efficacy have not yet been established in patients with a neurogenic cause for detrusor overactivity.

Other causes of frequent urination (treatment of heart failure or renal disease) should be assessed before treatment with fesoterodine. If urinary tract infection is present, an appropriate medical approach should be taken/antibacterial therapy should be started.

Angioedema
Angioedema has been reported with fesoterodine and has occurred after the first dose in some cases. Some cases may be associated with upper airway swelling and may be life-threatening. If angioedema occurs, fesoterodine should be discontinued and appropriate therapy should be promptly provided.

Potent CYP3A4 inducers
The concomitant use of fesoterodine with a potent CYP3A4 inducer (i.e. carbamazepine, rifampicin, phenobarbital, phenytoin, St John's Wort) is not recommended (see section 4.5).

QT prolongation
TOVIAZ should be used with caution in patients with risk for QT prolongation (e.g. hypokalaemia, bradycardia and concomitant administration of medicines known to prolong QT interval) and relevant pre-existing cardiac diseases (e.g. myocardial ischaemia, arrhythmia, congestive heart failure), (see section 4.8). This especially holds true when taking potent CYP3A4 inhibitors (see sections 4.2, 4.5 and 5.1).

Lactose
TOVIAZ 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 medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Pharmacological interactions
Caution should be exercised in coadministration of fesoterodine with other antimuscarinics and medicinal products with anticholinergic properties (e.g. amantadine, tri-cyclic antidepressants, certain neuroleptics) as this may lead to more pronounced therapeutic- and side-effects (e.g. constipation, dry mouth, drowsiness, urinary retention).

Fesoterodine may reduce the effect of medicinal products that stimulate the motility of the gastro-intestinal tract, such as metoclopramide.

Pharmacokinetic interactions
In vitro data demonstrate that the active metabolite of fesoterodine does not inhibit CYP1A2, 2B6, 2C8, 2C9, 2C19, 2D6, 2E1, or 3A4, or induce CYP1A2, 2B6, 2C9, 2C19, or 3A4 at clinically relevant plasma concentrations. Thus fesoterodine is unlikely to alter the clearance of medicinal products that are metabolised by these enzymes.

CYP3A4 inhibitors

Potent CYP3A4 inhibitors
Following inhibition of CYP3A4 by co-administration of ketoconazole 200 mg twice daily, C_{max} and AUC of the active metabolite of fesoterodine increased 2.0 and 2.3-fold in CYP2D6 extensive metabolisers and 2.1 and 2.5-fold in CYP2D6 poor metabolisers, respectively. Therefore, the maximum dose of fesoterodine should be restricted to 4 mg when used concomitantly with potent CYP3A4 inhibitors (e.g. atazanavir, clarithromycin, indinavir, itraconazole, ketoconazole, nefazodone, nelfinavir, ritonavir (and all ritonavir boosted PI-regimens), saquinavir and telithromycin (see sections 4.2 and 4.4).

Moderate CYP3A4 inhibitors
Following blockade of CYP3A4 by coadministration of the moderate CYP3A4 inhibitor fluconazole 200 mg twice a day for 2 days, C_{max} and AUC of the active metabolite of fesoterodine increased approximately 19% and 27%, respectively. No dosing adjustments are recommended in the presence of moderate CYP3A4 inhibitors (e.g., erythromycin, fluconazole, diltiazem, verapamil and grapefruit juice).

Weak CYP3A4 inhibitors
The effect of weak CYP3A4 inhibitors (e.g. cimetidine), was not examined; it is not expected to be in excess of the effect of moderate inhibitor.

CYP3A4 inducers
Following induction of CYP3A4 by coadministration of rifampicin 600 mg once a day, C_{max} and AUC of the active metabolite of fesoterodine decreased by approximately 70% and 75%, respectively, after oral administration of fesoterodine 8 mg.

Induction of CYP3A4 may lead to subtherapeutic plasma levels. Concomitant use with CYP3A4 inducers (e.g. carbamazepine, rifampicin, phenobarbital, phenytoin, St John's Wort) is not recommended (see section 4.4).

CYP2D6 inhibitors
The interaction with CYP2D6 inhibitors was not tested clinically. Mean C_{max} and AUC of the active metabolite are 1.7 and 2-fold higher, respectively, in CYP2D6 poor metabolisers as compared to extensive metabolisers. Co-administration of a potent CYP2D6 inhibitor may result in increased exposure and adverse events. A dose reduction to 4 mg may be needed (see section 4.4).

Oral contraceptives
Fesoterodine does not impair the suppression of ovulation by oral hormonal contraception. In the presence of fesoterodine there are no changes in the plasma concentrations of combined oral contraceptives containing ethinylestradiol and levonorgestrel.

Warfarin
A clinical study in healthy volunteers has shown that fesoterodine 8 mg once daily has no significant effect on the pharmacokinetics or the anticoagulant activity of a single dose of warfarin.

Paediatric population
Interaction studies have only been performed in adults.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no adequate data from the use of fesoterodine in pregnant women. Reproductive toxicity studies with fesoterodine in animals show minor embryotoxicity. In animal reproduction studies, oral administration of fesoterodine to pregnant mice and rabbits during organogenesis resulted in fetotoxicity at maternal exposures that were 6 and 3 times the maximum recommended human dose (MRHD), respectively, based on AUC (see section 5.3). The potential risk for humans is unknown. TOVIAZ is not recommended during pregnancy.

Breast-feeding
It is unknown whether fesoterodine/metabolites are excreted into human milk; therefore, breast-feeding is not recommended during treatment with TOVIAZ.

Fertility
No clinical trials have been conducted to assess the effect of fesoterodine on human fertility. Findings in mice at exposures approximately 5 to 19 times those at the MRHD show an effect on female fertility, however, the clinical implications of these animal findings are not known (see section 5.3). Women of child bearing potential should be made aware of the lack of human fertility data, and TOVIAZ should only be given after consideration of individual risks and benefits.

4.7 Effects on ability to drive and use machines

TOVIAZ has minor influence on the ability to drive and use machines.

Caution should be exercised when driving or using machines due to possible occurrence of side effects such as blurred vision, dizziness, and somnolence (see section 4.8).

4.8 Undesirable effects

Summary of the safety profile
The safety of fesoterodine was evaluated in placebo-controlled clinical studies in a total of 2859 patients with overactive bladder, of which 780 received placebo.

Due to the pharmacological properties of fesoterodine, treatment may cause mild to moderate antimuscarinic effects like dry mouth, dry eye, dyspepsia and constipation. Urinary retention may occur uncommonly.

Dry mouth, the only very common adverse reactions, occurred with a frequency of 28.8% in the fesoterodine group compared to 8.5% in the placebo group. The majority of adverse reactions occurred during the first month of treatment with the exception of cases classified as urinary retention or post void residual urine greater than 200 ml, which could occur after long term treatment and was more common in male than female subjects.

Tabulated list of adverse reactions

The table below gives the frequency of treatment emergent adverse reactions from placebo-controlled clinical trials and from post-marketing experience. The adverse reactions are reported in this table with the following frequency convention: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000).

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

System organ class	Very common	Common	Uncommon	Rare
Infections and infestations			Urinary tract infection	
Psychiatric disorders		Insomnia		Confusional state
Nervous system disorders		Dizziness; Headache	Dysgeusia; Somnolence	
Eye disorders		Dry eye	Blurred vision	
Ear and labyrinth disorders			Vertigo	
Cardiac disorders			Tachycardia; Palpitations	
Respiratory, thoracic and mediastinal disorders		Dry throat	Pharyngolaryngeal pain; Cough; Nasal dryness	
Gastrointestinal disorders	Dry mouth	Abdominal pain; Diarrhoea; Dyspepsia; Constipation; Nausea	Abdominal discomfort; Flatulence, Gastroesophageal reflux	Hypoaesthesia oral
Hepatobiliary disorders			ALT increased; GGT increased	
Skin and subcutaneous tissue disorders			Rash; Dry skin; Pruritus	Angioedema; Urticaria
Renal and urinary disorders		Dysuria	Urinary retention (including feeling of residual urine; micturition disorder); Urinary hesitation	
General disorders and administration site conditions			Fatigue	

Description of selected adverse reactions

In clinical trials of fesoterodine, cases of markedly elevated liver enzymes were reported with the occurrence frequency no different from the placebo group. The relation to fesoterodine treatment is unclear.

Electrocardiograms were obtained from 782 patients treated with 4 mg, 785 treated with 8 mg, 222 treated with 12 mg fesoterodine and 780 with placebo. The heart rate corrected QT interval in fesoterodine treated patients did not differ from that seen in placebo treated patients. The incidence rates of QTc ≥ 500 ms post baseline or QTc increase of ≥ 60 ms is 1.9%, 1.3%, 1.4% and 1.5%, for

fesoterodine 4 mg, 8 mg, 12 mg and placebo, respectively. The clinical relevance of these findings will depend on individual patient risk factors and susceptibilities present (see section 4.4).

Post-marketing cases of urinary retention requiring catheterisation have been described, generally within the first week of treatment with fesoterodine. They have mainly involved elderly (≥ 65 years) male patients with a history consistent with benign prostatic hyperplasia (see section 4.4).

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Overdose with antimuscarinics, including fesoterodine can result in severe anticholinergic effects. Treatment should be symptomatic and supportive. In the event of overdose, ECG monitoring is recommended; standard supportive measures for managing QT prolongation should be adopted. Fesoterodine has been safely administered in clinical studies at doses up to 28 mg/day.

In the event of fesoterodine overdose, treat with gastric lavage and give activated charcoal. Treat symptoms as follows:

- Severe central anticholinergic effects (e.g. hallucinations, severe excitation): treat with physostigmine
- Convulsions or pronounced excitation: treat with benzodiazepines
- Respiratory insufficiency: treat with artificial respiration
- Tachycardia: treat with beta-blockers
- Urinary retention: treat with catheterisation
- Mydriasis: treat with pilocarpine eye drops and/or place patient in dark room.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Urologicals, Urinary antispasmodics, ATC code: G04BD11.

Mechanism of action
Fesoterodine is a competitive, specific muscarinic receptor antagonist. It is rapidly and extensively hydrolysed by non-specific plasma esterases to the 5-hydroxymethyl derivative, its primary active metabolite, which is the main active pharmacological principle of fesoterodine.

Clinical efficacy and safety
The efficacy of fixed doses of fesoterodine 4 mg and 8 mg was evaluated in two Phase 3 randomised, double-blind, placebo-controlled, 12-week studies. Female (79%) and male (21%) patients with a mean age of 58 years (range 19-91 years) were included. A total of 33% of patients were ≥ 65 years of age and 11% were ≥ 75 years of age.

Fesoterodine treated patients had statistically significant mean reductions in the number of micturitions per 24 hours and in the number of urge incontinence episodes per 24 hours at the end of treatment compared to placebo. Likewise, the response rate (% of patients reporting that their condition has been “greatly improved” or “improved” using a 4-point Treatment Benefit Scale) was significantly greater with fesoterodine compared to placebo. Furthermore, fesoterodine improved the mean change in the voided volume per micturition, and the mean change in the number of continent days per week (see Table 1 below).

Table 1: Mean changes from baseline to end of treatment for primary and selected secondary endpoints

	Study 1				Study 2		
Parameter	**Placebo**	**Fesoterodine 4 mg**	**Fesoterodine 8 mg**	**Active comparator**	**Placebo**	**Fesoterodine 4 mg**	**Fesoterodine 8 mg**
Number of micturitions per 24 hours#							
	N=279	N=265	N=276	N=283	N=266	N=267	N=267
Baseline	12.0	11.6	11.9	11.5	12.2	12.9	12.0
Change from baseline	-1.02	-1.74	-1.94	-1.69	-1.02	-1.86	-1.94
p-value		<0.001	<0.001			0.032	<0.001
Responder rate (treatment response)#							
	N=279	N=265	N=276	N=283	N=266	N=267	N=267
Responder rate	53.4%	74.7%	79.0%	72.4%	45.1%	63.7%	74.2%
p-value		<0.001	<0.001			<0.001	<0.001
Number of urge incontinence episodes per 24 hours							
	N=211	N=199	N=223	N=223	N=205	N=228	N=218
Baseline	3.7	3.8	3.7	3.8	3.7	3.9	3.9
Change from baseline	-1.20	-2.06	-2.27	-1.83	-1.00	-1.77	-2.42
p-value		0.001	<0.001			0.003	<0.001
Number of continent days per week							
	N=211	N=199	N=223	N=223	N=205	N=228	N=218
Baseline	0.8	0.8	0.6	0.6	0.6	0.7	0.7
Change from baseline	2.1	2.8	3.4	2.5	1.4	2.4	2.8
p-value		0.007	<0.001			<0.001	<0.001
Voided volume per micturition (ml)							
	N=279	N=265	N=276	N=283	N=266	N=267	N=267
Baseline	150	160	154	154	159	152	156
Change from baseline	10	27	33	24	8	17	33
p-value		<0.001	<0.001			0.150	<0.001

primary end points

Cardiac electrophysiology

The effect of fesoterodine 4 mg and 28 mg on the QT interval was thoroughly evaluated in a double-blind, randomised, placebo- and positive-controlled (moxifloxacin 400 mg) parallel group study with once-daily treatment over a period of 3 days in 261 male and female subjects aged 45 to

65 years. Change from baseline in QTc based on the Fridericia correction method did not show any differences between the active treatment and placebo group.

Paediatric population
Fesoterodine was evaluated in a randomised, open-label study consisting of a 12-week efficacy phase study followed by a 12-week safety extension phase in paediatric patients from 6 years to 17 years of age with neurogenic detrusor overactivity. Two cohorts were studied. In the Cohort 1, 124 patients weighing > 25 kg received a fixed dose of fesoterodine 4 mg or 8 mg tablets once-daily or active comparator oxybutynin XL tablets. In the safety extension phase, patients randomised to active comparator tablets were switched to fesoterodine 4 mg or 8 mg tablets (allocated by the investigator). In the Cohort 2, 57 patients weighing ≤ 25 kg received a fixed dose of fesoterodine 2 mg or 4 mg investigational beads-in-capsule (BIC) formulation once daily. In the safety extension phase, patients continued on the dose of fesoterodine to which they had been randomised. For study inclusion, patients were required to have stable neurological disease and clinically or urodynamically-demonstrated neurogenic detrusor overactivity (see section 4.2).

The primary efficacy endpoint for both Cohorts was the mean change from baseline in maximum cystometric bladder capacity (MCBC) at Week 12. Treatment with fesoterodine 4 mg or 8 mg tablets resulted in improvements from baseline to Week 12 in the primary efficacy endpoint, MCBC, for paediatric patients in Cohort 1, with numerically higher changes from baseline for fesoterodine 8 mg tablets than for fesoterodine 4 mg tablets. Treatment with fesoterodine 2 mg and 4 mg BIC resulted in improvements from baseline to Week 12 in the primary efficacy endpoint, MCBC, for paediatric patients in Cohort 2, with numerically higher changes from baseline for fesoterodine 4 mg BIC than for fesoterodine 2 mg BIC.

Table 2: Mean baseline and change from baseline to week 12 maximum cystometric bladder capacity (mL)

	Cohort 1 (body weight > 25 kg)			**Cohort 2 (body weight ≤ 25 kg)**	
	Feso 4 mg tablet	**Feso 8 mg tablet**	**Oxybutynin XL**	**Feso 2 mg BIC**	**Feso 4 mg BIC**
	N = 41	**N = 41**	**N = 38**	**N = 25**	**N = 28**
Baseline	195.1	173.3	164.1	131.4	126.7
Change from baseline (95% CI)[a]	58.12 (28.84, 87.39)	83.36 (54.22,112.49)	87.17 (56.82,117.53)	23.49 (3.03, 43.95)	40.17 (20.84, 59.50)
p-value vs. baseline[a]	0.0001	<.0001	<.0001	--[b]	--[b]

Abbreviations: BIC = beads-in-capsule; CI = confidence interval; Feso = fesoterodine, N = number of patients with a non-missing baseline measurement; vs. = versus.
Baseline is defined as the last available measurement prior to the start of treatment.

a. Based on an analysis of covariance model with terms for treatment group, baseline maximum cystometric bladder capacity and baseline weight. Last observation carried forward/baseline observation was used for imputing missing values.
b. No hypothesis testing was planned for Cohort 2; therefore, no p-values are presented.

Secondary endpoints
Treatment with fesoterodine 4 mg or 8 mg tablets resulted in statistically significant improvements in the urodynamic measure secondary endpoint bladder volume at first involuntary detrusor contraction.

The most commonly reported adverse reactions in the efficacy phase were diarrhoea, dry mouth, constipation, abdominal pain (including upper abdominal pain) and headache. These mild to moderate adverse reactions are consistent with the pharmacological, antimuscarinic properties of fesoterodine. Increases in heart rate were observed in patients who received TOVIAZ which were not associated

with clinical symptoms. Overall, the safety profile in paediatric patients with neurogenic detrusor overactivity was similar to that observed in adults with overactive bladder syndrome.

5.2 Pharmacokinetic properties

Absorption
After oral administration, due to rapid and extensive hydrolysis by non-specific plasma esterases, fesoterodine was not detected in plasma.

Bioavailability of the active metabolite is 52%. After single or multiple-dose oral administration of fesoterodine in doses from 4 mg to 28 mg, plasma concentrations of the active metabolite are proportional to the dose. The steady-state exposures of 5-HMT in healthy adult subjects following fesoterodine 4 mg and 8 mg tablets once daily are summarised in Table 3.

Table 3: Summary of geometric mean [% CV] pharmacokinetic parameters for the active metabolite after steady-state dosing of fesoterodine in healthy adult subjects, 18 years to 50 years of age

Dosage/Formulation	N	$C_{max,ss}$ (ng/mL)	$AUC_{tau,ss}$ (ng*h/mL)
4 mg QD/tablet	6	1.71 (74.9)	16.39 (69.8)
8 mg QD/tablet	6	4.66 (43.3)	46.51 (46.8)

Abbreviations: $AUC_{tau,ss}$ = steady-state area under the concentration time curve over the 24 hour dosing interval; $C_{max,ss}$ = steady-state maximum plasma concentration; CV = coefficient of variation; N = number of patients with PK data; QD = once daily.

Maximum plasma levels are reached after approximately 5 hours. Therapeutic plasma levels are achieved after the first administration of fesoterodine. No accumulation occurs after multiple-dose administration.

Distribution
Plasma protein binding of the active metabolite is low with approximately 50% bound to albumin and alpha-1-acid glycoprotein. The mean steady-state volume of distribution following intravenous infusion of the active metabolite is 169 l.

Biotransformation
After oral administration, fesoterodine is rapidly and extensively hydrolysed to its active metabolite. The active metabolite is further metabolised in the liver to its carboxy, carboxy-N-desisopropyl, and N-desisopropyl metabolite with involvement of CYP2D6 and CYP3A4. None of these metabolites contribute significantly to the antimuscarinic activity of fesoterodine. Mean C_{max} and AUC of the active metabolite are 1.7 and 2-fold higher, respectively, in CYP2D6 poor metabolisers as compared to extensive metabolisers.

Elimination
Hepatic metabolism and renal excretion contribute significantly to the elimination of the active metabolite. After oral administration of fesoterodine, approximately 70% of the administered dose was recovered in urine as the active metabolite (16%), carboxy metabolite (34%), carboxy-N-desisopropyl metabolite (18%), or N-desisopropyl metabolite (1%), and a smaller amount (7%) was recovered in faeces. The terminal half-life of the active metabolite following oral administration is approximately 7 hours and is absorption rate-limited.

Age and gender
No dose adjustment is recommended in these subpopulations. The pharmacokinetics of fesoterodine are not significantly influenced by age and gender.

Paediatric population

In paediatric patients, from 6 years to 17 years of age with neurogenic detrusor overactivity weighing 35 kg with CYP2D6 extensive metaboliser status receiving fesoterodine tablets, the mean values of apparent oral clearance, volume of distribution and absorption rate constant of 5-HMT are estimated to be approximately 72 L/h, 68 L and 0.09 h^{-1}, respectively. The T_{max} and half-life of 5-HMT are estimated to be approximately 2.55 h and 7.73 h, respectively. Like adults, the 5-HMT exposure in CYP2D6 poor metabolisers was estimated to be approximately 2-fold higher compared with extensive metabolisers.

The post-hoc estimates of steady-state exposures of 5-HMT in paediatric patients following fesoterodine 4 mg and 8 mg tablets once daily are summarised in Table 4.

Table 4: Summary of geometric mean [% CV] pharmacokinetic parameters for the active metabolite after steady-state dosing of fesoterodine in paediatric patients with NDO or OAB, weighing > 25 kg

Age	Dosage/Formulation	N	$C_{max,ss}$ (ng/mL)	$AUC_{tau,ss}$ (ng*h/mL)
6 to 17 years (patients with NDO)	4 mg QD/tablet	32	4.88 (48.2)	59.1 (51.7)
	8 mg QD/tablet	39	8.47 (41.6)	103 (46.2)
8 to 17 years (patients with NDO or OAB)	8 mg QD/tablet[1]	21	7.15 (39.5)	86.4 (44.0)

[1] dosing was initiated at 4 mg QD for 4 weeks and escalated to 8 mg QD for the next 4 weeks.
Abbreviations: $AUC_{tau,ss}$ = steady-state area under the concentration time curve over the 24 hour dosing interval; $C_{max,ss}$ = steady-state maximum plasma concentration; CV = coefficient of variation; N = number of patients with PK data; QD = once daily.

Renal impairment
In patients with mild or moderate renal impairment (GFR 30 – 80 ml/min), C_{max} and AUC of the active metabolite increased up to 1.5 and 1.8-fold, respectively, as compared to healthy subjects. In patients with severe renal impairment (GFR < 30 ml/min), C_{max} and AUC are increased 2.0 and 2.3-fold, respectively.

Hepatic impairment
In patients with moderate hepatic impairment (Child Pugh B), C_{max} and AUC of the active metabolite increased 1.4 and 2.1-fold, respectively, as compared to healthy subjects. Pharmacokinetics of fesoterodine in patients with severe hepatic impairment have not been studied.

5.3 Preclinical safety data

In non-clinical safety pharmacology, general toxicity, genotoxicity and carcinogenicity studies no clinically relevant effects have been observed, except those related to the pharmacological effect of the active substance.

Reproduction studies have shown minor embryotoxicity at doses close to maternally toxic ones (increased number of resorptions, pre-implantation and post-implantation losses).

Supratherapeutic concentrations of the active metabolite of fesoterodine, have been shown to inhibit K^+ current in cloned human ether-à-go-go-related gene (hERG) channels and prolong action potential duration (70% and 90% repolarisation) in canine isolated Purkinje fibres. However in conscious dogs, the active metabolite had no effect on the QT interval and QTc interval at plasma exposures at least 33-fold higher than mean peak free plasma concentration in human subjects who are extensive metabolisers and 21-fold higher than measured in subjects who are poor CYP2D6 metabolisers after fesoterodine 8 mg once daily.

In a study of fertility and early embryonic development in mice, fesoterodine had no effect on male reproductive function or fertility at doses up to 45 mg/kg/day. At 45 mg/kg/day, a lower number of corpora lutea, implantation sites and viable foetuses was observed in female mice administered fesoterodine for 2 weeks prior to mating and continuing through day 7 of gestation. The maternal No-Observed-Effect Level (NOEL) and the NOEL for effects on reproduction and early embryonic development were both 15 mg/kg/day. Based on AUC, the systemic exposure was 0.6 to 1.5 times higher in mice than in humans at the MRHD, whereas based on peak plasma concentrations, the exposure in mice was 5 to 9 times higher.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core
Xylitol
Lactose monohydrate
Microcrystalline cellulose
Hypromellose
Glycerol dibehenate
Talc

Film-coating
Poly(vinyl alcohol)
Titanium dioxide (E171)
Macrogol (3350)
Talc
Soya lecithin
Indigo carmine aluminium lake (E132)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Do not store above 25°C.
Store in the original package in order to protect from moisture.

6.5 Nature and contents of container

TOVIAZ 4 mg and 8 mg tablets are packed in aluminium-aluminium blisters in cartons containing 7, 14, 28, 30, 56, 84, 98 or 100 tablets. In addition, TOVIAZ 4 mg and 8 mg tablets are also packed in HDPE bottles containing 30 or 90 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

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

7. MARKETING AUTHORISATION HOLDER

Pfizer Europe MA EEIG
Boulevard de la Plaine 17
1050 Bruxelles
Belgium

8. MARKETING AUTHORISATION NUMBER(S)

TOVIAZ 4 mg tablets
EU/1/07/386/001-005
EU/1/07/386/011
EU/1/07/386/013-014
EU/1/07/386/017
EU/1/07/386/019

TOVIAZ 8 mg tablets
EU/1/07/386/006-010
EU/1/07/386/012
EU/1/07/386/015-016
EU/1/07/386/018
EU/1/07/386/020

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 20 April 2007
Date of latest renewal: 15 March 2012

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER(S)RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturers responsible for batch release

Pfizer Manufacturing Deutschland GmbH
Betriebsstätte Freiburg
Mooswaldallee 1
79090 Freiburg
Germany

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

Outer carton 4 mg

1. NAME OF THE MEDICINAL PRODUCT

TOVIAZ 4 mg prolonged-release tablets
fesoterodine fumarate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 4 mg fesoterodine fumarate

3. LIST OF EXCIPIENTS

Contains lactose and soya lecithin: see the package leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

7 prolonged-release tablets
14 prolonged-release tablets
28 prolonged-release tablets
30 prolonged-release tablets
56 prolonged-release tablets
84 prolonged-release tablets
98 prolonged-release tablets
100 prolonged-release tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral use.

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

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Sealed pack
Do not use if box has been opened

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Do not store above 25ºC.
Store in the original package in order to protect from moisture.

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

Pfizer Europe MA EEIG
Boulevard de la Plaine 17
1050 Bruxelles
Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/07/386/001 7 prolonged-release tablets
EU/1/07/386/002 14 prolonged-release tablets
EU/1/07/386/003 28 prolonged-release tablets
EU/1/07/386/019 30 prolonged-release tablets
EU/1/07/386/004 56 prolonged-release tablets
EU/1/07/386/005 98 prolonged-release tablets
EU/1/07/386/011 84 prolonged-release tablets
EU/1/07/386/017 100 prolonged-release tablets

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

TOVIAZ 4 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

Blister label 4 mg

1. NAME OF THE MEDICINAL PRODUCT

TOVIAZ 4 mg prolonged-release tablets
fesoterodine fumarate

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Pfizer Europe MA EEIG (as MA Holder logo)

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

Monday
Tuesday
Wednesday
Thursday
Friday
Saturday
Sunday

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING

Immediate packaging HDPE Bottle – 4 mg

1. NAME OF THE MEDICINAL PRODUCT

TOVIAZ 4 mg prolonged-release tablets
fesoterodine fumarate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 4 mg fesoterodine fumarate

3. LIST OF EXCIPIENTS

Contains lactose and soya lecithin: see the package leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

30 prolonged-release tablets
90 prolonged-release tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral use.

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

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Do not store above 25ºC.
Store in the original package in order to protect from moisture.

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

Pfizer Europe MA EEIG
Boulevard de la Plaine 17
1050 Bruxelles
Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/07/386/013 30 prolonged-release tablets
EU/1/07/386/014 90 prolonged-release tablets

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

Outer carton 8 mg

1. NAME OF THE MEDICINAL PRODUCT

TOVIAZ 8 mg prolonged-release tablets
fesoterodine fumarate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 8 mg fesoterodine fumarate

3. LIST OF EXCIPIENTS

Contains lactose and soya lecithin: see the package leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

7 prolonged-release tablets
14 prolonged-release tablets
28 prolonged-release tablets
30 prolonged-release tablets
56 prolonged-release tablets
84 prolonged-release tablets
98 prolonged-release tablets
100 prolonged-release tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral use.

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

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Sealed pack
Do not use if box has been opened

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Do not store above 25ºC.
Store in the original package in order to protect from moisture.

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

Pfizer Europe MA EEIG
Boulevard de la Plaine 17
1050 Bruxelles
Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/07/386/006 7 prolonged-release tablets
EU/1/07/386/007 14 prolonged-release tablets
EU/1/07/386/008 28 prolonged-release tablets
EU/1/07/386/020 30 prolonged-release tablets
EU/1/07/386/009 56 prolonged-release tablets
EU/1/07/386/010 98 prolonged-release tablets
EU/1/07/386/012 84 prolonged-release tablets
EU/1/07/386/018 100 prolonged-release tablets

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

TOVIAZ 8 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

Blister label 8 mg

1. NAME OF THE MEDICINAL PRODUCT

TOVIAZ 8 mg prolonged-release tablets
fesoterodine fumarate

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Pfizer Europe MA EEIG (as MA Holder logo)

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

Monday
Tuesday
Wednesday
Thursday
Friday
Saturday
Sunday

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

Immediate Packaging HDPE Bottle – 8 mg

1. NAME OF THE MEDICINAL PRODUCT

TOVIAZ 8 mg prolonged-release tablets
fesoterodine fumarate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 8 mg fesoterodine fumarate

3. LIST OF EXCIPIENTS

Contains lactose and soya lecithin: see the package leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

30 prolonged-release tablets
90 prolonged-release tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral use.

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

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Do not store above 25ºC.
Store in the original package in order to protect from moisture.

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

Pfizer Europe MA EEIG
Boulevard de la Plaine 17
1050 Bruxelles
Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/07/386/015 30 prolonged-release tablets
EU/1/07/386/016 90 prolonged-release tablets

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

B. PACKAGE LEAFLET

Package leaflet: Information for the user

TOVIAZ 4 mg prolonged-release tablets
TOVIAZ 8 mg prolonged-release tablets
fesoterodine fumarate

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- 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 only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What TOVIAZ is and what it is used for

TOVIAZ contains an active substance called fesoterodine fumarate, and is a so called antimuscarinic treatment which reduces the activity of an overactive bladder and it is used in adults to treat the symptoms.

TOVIAZ treats the symptoms of an overactive bladder such as
- not being able to control when you empty your bladder (called urgency incontinence)
- suddenly needing to empty your bladder (called urgency)
- having to empty your bladder more often than usual (called increased urinary frequency)

2. What you need to know before you take TOVIAZ

Do not take TOVIAZ:
- if you are allergic to fesoterodine or to peanut or soya or to any of the other ingredients of TOVIAZ (listed in section 6) (see section 2, “TOVIAZ contains lactose and soya oil”)
- if you are not able to completely empty your bladder (urinary retention)
- if your stomach empties slowly (gastric retention)
- if you have an eye disease called narrow angle glaucoma (high pressure in the eye), which is not under control
- if you have excessive weakness of the muscles (myasthenia gravis)
- if you have ulceration and inflammation of the colon (severe ulcerative colitis)
- if you have an abnormally large or distended colon (toxic megacolon)
- if you have severe liver problems.
- if you have kidney problems or moderate to severe liver problems and are taking medicines containing any of the following active substances: itraconazole or ketoconazole (used to treat fungal infections), ritonavir, atazanavir, indinavir, saquinavir or nelfinavir (antiviral medicine for treating HIV), clarithromycin or telithromycin (used to treat bacterial infections) and nefazodone (used to treat depression)

Warnings and Precautions
Fesoterodine may not always be suitable for you. Talk to your doctor before taking TOVIAZ, if any of the following apply to you:
- if you have difficulties in completely emptying your bladder (for example due to prostate enlargement)
- if you ever experience decreased bowel movements or suffer from severe constipation
- if you are being treated for an eye disease called narrow angle glaucoma
- if you have serious kidney or liver problems, your doctor may need to adjust your dose
- if you have a disease called autonomic neuropathy which you notice from symptoms such as changes in your blood pressure or disorders in the bowel or sexual function
- if you have a gastrointestinal disease that affects the passage and/or digestion of food
- if you have heartburn or belching.
- if you have an infection of the urinary tract, your doctor may need to prescribe some antibiotics

Heart problems: Talk to your doctor if you suffer from any of the following conditions
- you have an ECG (heart tracing) abnormality known as QT prolongation or you are taking any medicine known to cause this
- you have a slow heart rate (bradycardia)
- you suffer from heart disease such as myocardial ischaemia (reduced blood flow to the heart muscle), irregular heartbeat or heart failure
- you have hypokalaemia, which is a manifestation of abnormally low levels of potassium in your blood.

Children and adolescents
Do not give this medicine to children and adolescents below 18 years of age because it is yet to be established whether it would work for them and whether it would be safe.

Other medicines and TOVIAZ
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. Your doctor will tell you whether you can take TOVIAZ with other medicines.

Please inform your doctor if you are taking medicines according to the following list. Taking them at the same time as fesoterodine may make side effects such as dry mouth, constipation, difficulty in completely emptying your bladder or drowsiness more serious or occur more often.
- medicines containing the active substance amantadine (used to treat Parkinson's disease).
- certain medicines used to enhance gastrointestinal motility or to relieve stomach cramps or spasm and to prevent travel sickness like medicines containing metoclopramide.
- certain medicines used to treat psychiatric diseases, like anti-depressives and neuroleptics.

Please also inform your doctor if you are taking any of the following medicines:
- medicines containing any of the following active substances may increase the break-down of fesoterodine and thus decrease its effect: St. John's Wort (herbal medicinal product), rifampicin (used to treat bacterial infections), carbamazepine, phenytoin and phenobarbital (used, among others, to treat epilepsy).
- medicines containing any of the following active substances may increase the blood levels of fesoterodine: itraconazole or ketoconazole (used to treat fungal infections), ritonavir, atazanavir, indinavir, saquinavir or nelfinavir (antiviral medicine for treating HIV), clarithromycin or telithromycin (used to treat bacterial infections), nefazodone (used to treat depression), fluoxetine or paroxetine (used to treat depression or anxiety), bupropion (used for smoking cessation or to treat depression), quinidine (used to treat arrhythmias) and cinacalcet (used to treat hyperparathyroidism).
- medicines containing the active substance methadone (used in the treatment of severe pain and abuse problems).

Pregnancy and breast-feeding
You should not take TOVIAZ if you are pregnant, as the effects of fesoterodine on pregnancy and the unborn baby are not known.

It is not known whether fesoterodine is excreted into human milk; therefore, do not breast-feed during treatment with TOVIAZ.

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Driving and using machines
TOVIAZ can cause blurred vision, dizziness, and sleepiness. If you experience any of these effects, do not drive or use any tools or machines.

TOVIAZ contains lactose and soya oil
TOVIAZ 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.

TOVIAZ contains soya oil. If you are allergic to peanut or soya, do not use this medicinal product.

3. How to take TOVIAZ

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

The recommended starting dose of TOVIAZ is one 4 mg tablet a day. Based on how you respond to the medicine, your doctor may prescribe you a higher dose; one 8 mg tablet a day.

You should swallow your tablet whole with a glass of water. Do not chew the tablet. TOVIAZ can be taken with or without food.

To help you remember to take your medicine, you may find it easier to take it at the same time every day.

If you take more TOVIAZ than you should
If you have taken more tablets than you have been told to take, or if someone else accidentally takes your tablets, contact your doctor or hospital for advice immediately. Show them your pack of tablets.

If you forget to take TOVIAZ
If you forget to take a tablet, take your tablet as soon as you remember, but do not take more than one tablet in one day. Do not take a double dose to make up for a forgotten tablet.

If you stop taking TOVIAZ
Do not stop taking TOVIAZ without talking to your doctor, as your symptoms of overactive bladder may come back again or become worse once you stop taking TOVIAZ.

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

4. Possible side effects

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

Some side effects could be serious
Serious allergic reactions including angioedema occurred rarely. You should stop taking TOVIAZ and contact your doctor immediately if you develop swelling of the face, mouth or throat as this may be life-threatening.

Other side effects

Very common (may affect more than 1 in 10 people)
You may get a dry mouth. This effect is usually mild or moderate. This may lead to a greater risk of dental caries. Therefore, you should brush your teeth regularly twice daily and see a dentist when in doubt.

Common (may affect up to 1 in 10 people)
- dry eye
- constipation
- trouble digesting food (dyspepsia)
- straining or pain when emptying the bladder (dysuria)
- dizziness
- headache
- pain in the stomach
- diarrhoea
- feeling sick (nausea)
- difficulty sleeping (insomnia)
- dry throat

Uncommon (may affect up to 1 in 100 people)
- urinary tract infection
- sleepiness (somnolence)
- difficulty tasting (dysgeusia)
- vertigo
- rash
- dry skin
- itching
- an uncomfortable feeling in the stomach
- wind (flatulence)
- difficulty in completely emptying the bladder (urinary retention)
- delay in passing urine (urinary hesitation)
- extreme tiredness (fatigue)
- increased heart beat (tachycardia)
- palpitations
- liver problems
- cough
- nasal dryness
- throat pain
- stomach acid reflux
- blurred vision

Rare (may affect up to 1 in 1,000 people)
- urticaria
- confusion
- numbness around mouth (hypoaesthesia oral)

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system

listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store TOVIAZ

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and the blister after "EXP". The expiry date refers to the last day of that month.

Do not store above 25°C.

Store in the original package in order to protect from moisture.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What TOVIAZ contains

- The active substance is fesoterodine fumarate.

TOVIAZ 4 mg
Each prolonged-release tablet contains 4 mg fesoterodine fumarate, equivalent to 3.1 mg of fesoterodine.
TOVIAZ 8 mg
Each prolonged-release tablet contains 8 mg fesoterodine fumarate, equivalent to 6.2 mg of fesoterodine.

- The other ingredients are:

The tablet core: xylitol, lactose monohydrate, microcrystalline cellulose, hypromellose, glycerol dibehenate, talc.
The coating: polyvinyl alcohol, titanium dioxide (E171), macrogol (3350), talc, soya lecithin, indigo carmine aluminium lake (E132).

What TOVIAZ looks like and contents of the pack

TOVIAZ 4 mg prolonged-release tablets are light blue, oval, curved outwards on both sides, film-coated tablets, and engraved on one side with the letters 'FS'.

TOVIAZ 8 mg prolonged-release tablets are blue, oval, curved outwards on both sides, film-coated tablets, and engraved on one side with the letters 'FT'.

TOVIAZ is available in blister packs of 7, 14, 28, 30, 56, 84, 98 and 100 prolonged-release tablets. In addition, TOVIAZ is also available in HDPE bottles containing 30 or 90 tablets.

Please note that not all the above pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:

Pfizer Europe MA EEIG
Boulevard de la Plaine 17
1050 Bruxelles
Belgium

Manufacturer:

Pfizer Manufacturing Deutschland GmbH
Betriebsstätte Freiburg
Mooswaldallee 1
79090 Freiburg
Germany

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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Luxembourg/Luxemburg
Pfizer NV/SA
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Slovenija
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This leaflet was last revised in

Other sources of information
Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.