HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use TOVIAZ safely and effectively. See full prescribing information for TOVIAZ.

Toviaz® (fesoterodine fumarate)
For oral administration
Initial U.S. Approval: 2008

----------RECENT MAJOR CHANGES----------
Warnings and Precautions: Concomitant Administration with CYP3A4 Inhibitors (5.8) 10/2011
Warnings and Precautions: Central Nervous System Effects (5.5) 8/2012

----------INDICATIONS AND USAGE----------
Toviaz is a muscarinic antagonist indicated for the treatment of overactive bladder with symptoms of urge urinary incontinence, urgency, and frequency. (1)

----------DOSAGE AND ADMINISTRATION----------
The recommended starting dose of Toviaz is 4 mg once daily. Based upon individual response and tolerability, the dose may be increased to 8 mg once daily. (2)
The daily dose of Toviaz should not exceed 4 mg in the following populations:
- Patients with severe renal impairment (CL_{CR} <30 mL/min) (2)
- Patients taking potent CYP3A4 inhibitors, such as ketoconazole, itraconazole, and clarithromycin. (2)

Toviaz is not recommended for use in patients with severe hepatic impairment (Child-Pugh C). (2)
Toviaz should be taken with liquid and swallowed whole. Toviaz can be administered with or without food, and should not be chewed, divided, or crushed. (2)

----------DOSAGE FORMS AND STRENGTHS----------
Toviaz 4 mg extended-release tablets are light blue, oval, biconvex, film-coated, and engraved with "FS" on one side. (3)
Toviaz 8 mg extended-release tablets are blue, oval, biconvex, film-coated, and engraved with "FT" on one side. (3)

----------CONTRAINDICATIONS----------
Toviaz is contraindicated in patients with urinary retention, gastric retention, or uncontrolled narrow-angle glaucoma. Toviaz is also contraindicated in patients with known hypersensitivity to the drug or its ingredients or to tolterodine tartrate tablets or tolterodine tartrate extended-release capsules. (4)

----------WARNINGS AND PRECAUTIONS----------
- Angioedema of the face, lips, tongue, and/or larynx has been reported with fesoterodine. (5.1).
- Toviaz should be administered with caution to patients with clinically significant bladder outlet obstruction because of the risk of urinary retention. (5.2)
- Toviaz, like other antimuscarinic drugs, should be used with caution in patients with decreased gastrointestinal motility, such as those with severe constipation. (5.3)
- Toviaz should be used with caution in patients being treated for narrow-angle glaucoma, and only where the potential benefits outweigh the risks (5.4)
- Central Nervous System Effects: Somnolence has been reported with Toviaz. Advise patients not to drive or operate heavy machinery until they know how Toviaz affects them (5.5)
- Toviaz should be used with caution in patients with myasthenia gravis, a disease characterized by decreased cholinergic activity at the neuromuscular junction. (5.9)

----------ADVERSE REACTIONS----------
The most frequently reported adverse events (≥4%) for Toviaz were: dry mouth (placebo, 7%; Toviaz 4 mg, 19%; Toviaz 8 mg, 35%) and constipation (placebo, 2%; Toviaz 4 mg, 4%; Toviaz 8 mg, 6%). (6)
To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc at 1-800-438-1985 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch.*

----------USE IN SPECIFIC POPULATIONS----------
- *Pregnancy and Nursing Mothers:* Toviaz should be used during pregnancy only if the potential benefit outweighs the potential risk to the fetus. (8.1) Toviaz should not be administered during nursing unless the potential benefit outweighs the potential risk to the neonate. (8.3)
- *Pediatric Use:* The safety and effectiveness of Toviaz in pediatric patients have not been established. (8.4)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 08/2012

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Toviaz® is a muscarinic antagonist indicated for the treatment of overactive bladder with symptoms of urge urinary incontinence, urgency, and frequency.

2 DOSAGE AND ADMINISTRATION

The recommended starting dose of Toviaz is 4 mg once daily. Based upon individual response and tolerability, the dose may be increased to 8 mg once daily.

The daily dose of Toviaz should not exceed 4 mg in the following populations:

- Patients with severe renal impairment (CL_{CR} <30 mL/min).
- Patients taking potent CYP3A4 inhibitors, such as ketoconazole, itraconazole, and clarithromycin.

Toviaz is not recommended for use in patients with severe hepatic impairment (Child-Pugh C) [*see Warnings and Precautions (5.6, 5.8, 5.9); Use in Specific Populations (8.6, 8.7); and Drug Interactions (7.2)*].

Toviaz should be taken with liquid and swallowed whole. Toviaz can be administered with or without food, and should not be chewed, divided, or crushed.

3 DOSAGE FORMS AND STRENGTHS

Toviaz (fesoterodine fumarate) extended-release tablets 4 mg are light blue, oval, biconvex, film-coated, and engraved with "FS" on one side.

Toviaz (fesoterodine fumarate) extended-release tablets 8 mg are blue, oval, biconvex, film-coated, and engraved with "FT" on one side.

4 CONTRAINDICATIONS

Toviaz is contraindicated in patients with urinary retention, gastric retention, or uncontrolled narrow-angle glaucoma. Toviaz is also contraindicated in patients with known hypersensitivity to the drug or its ingredients, or to tolterodine tartrate tablets or tolterodine tartrate extended-release capsules [*see Clinical Pharmacology (12.1)*].

5 WARNINGS AND PRECAUTIONS

5.1 Angioedema: Angioedema of the face, lips, tongue, and/or larynx has been reported with fesoterodine. In some cases angioedema occurred after the first dose. Angioedema associated with upper airway swelling may be life-threatening. If involvement of the tongue, hypopharynx, or larynx occurs, fesoterodine should be promptly discontinued and appropriate therapy and/or measures to ensure a patent airway should be promptly provided.

5.2 Bladder Outlet Obstruction: Toviaz should be administered with caution to patients with clinically significant bladder outlet obstruction because of the risk of urinary retention [*see Contraindications (4)*].

5.3 Decreased Gastrointestinal Motility: Toviaz, like other antimuscarinic drugs, should be used with caution in patients with decreased gastrointestinal motility, such as those with severe constipation.

5.4 Controlled Narrow-Angle Glaucoma: Toviaz should be used with caution in patients being treated for narrow-angle glaucoma, and only where the potential benefits outweigh the risks [*see Contraindications (4)*].

5.5 **Central Nervous System Effects:** Toviaz is associated with anticholinergic central nervous sytem (CNS) effects [see Adverse Reactions (6.2)]. A variety of CNS anticholinergic effects have been reported, including headache, dizziness, and somnolence. Patients should be monitored for signs of anticholinergic CNS effects, particularly after beginning treatment or increasing the dose. Advise patients not to drive or operate heavy machinery until they know how Toviaz affects them. If a patient experiences anticholinergic CNS effects, dose reduction or drug discontinuation should be considered.

5.6 Hepatic Impairment: Toviaz has not been studied in patients with severe hepatic impairment and therefore is not recommended for use in this patient population [*see Use in Specific Populations (8.7) and Dosage and Administration (2)*].

5.7 Renal Impairment: Doses of Toviaz greater than 4 mg are not recommended in patients with severe renal impairment [*see Use In Specific Populations (8.6) and Dosage and Administration (2)*].

5.8 Concomitant Administration with CYP3A4 Inhibitors: Doses of Toviaz greater than 4 mg are not recommended in patients taking a potent CYP3A4 inhibitor (e.g., ketoconazole, itraconazole, clarithromycin).

No dosing adjustments are recommended in the presence of moderate CYP3A4 inhibitors (e.g., erythromycin, fluconazole, diltiazem, verapamil and grapefruit juice).

While the effect of weak CYP3A4 inhibitors (e.g. cimetidine) was not examined by clinical study, some pharmacokinetic interaction is expected, albeit less than that observed with moderate CYP3A4 inhibitors [*see Drug Interactions (7.2) and Dosage and Administration (2)*].

5.9 Myasthenia Gravis: Toviaz should be used with caution in patients with myasthenia gravis, a disease characterized by decreased cholinergic activity at the neuromuscular junction.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience: The safety of Toviaz was evaluated in Phase 2 and 3 controlled trials in a total of 2859 patients with overactive bladder, of which 2288 were treated with fesoterodine. Of this total, 782 received Toviaz 4 mg/day, and 785 received Toviaz 8 mg/day in Phase 2 or 3 studies with treatment periods of 8 or 12 weeks. Approximately 80% of these patients had >10 weeks exposure to Toviaz in these trials.

A total of 1964 patients participated in two 12-week, Phase 3 efficacy and safety studies and subsequent open-label extension studies. In these two studies combined, 554 patients received Toviaz 4 mg/day and 566 patients received Toviaz 8 mg/day.

In Phase 2 and 3 placebo-controlled trials combined, the incidences of serious adverse events in patients receiving placebo, Toviaz 4 mg, and Toviaz 8 mg were 1.9%, 3.5%, and 2.9%, respectively. All serious adverse events were judged to be not related or unlikely to be related to study medication by the investigator, except for four patients receiving Toviaz who reported one serious adverse event each: angina, chest pain, gastroenteritis, and QT prolongation on ECG.

The most commonly reported adverse event in patients treated with Toviaz was dry mouth. The incidence of dry mouth was higher in those taking 8 mg/day (35%) and in those taking 4 mg/day (19%), as compared to placebo

(7%). Dry mouth led to discontinuation in 0.4%, 0.4%, and 0.8% of patients receiving placebo, Toviaz 4 mg, and Toviaz 8 mg, respectively. For those patients who reported dry mouth, most had their first occurrence of the event within the first month of treatment.

The second most commonly reported adverse event was constipation. The incidence of constipation was 2% in those taking placebo, 4% in those taking 4 mg/day, and 6% in those taking 8 mg/day.

Table 1 lists adverse events, regardless of causality, that were reported in the combined Phase 3, randomized, placebo-controlled trials at an incidence greater than placebo and in 1% or more of patients treated with Toviaz 4 or 8 mg once daily for up to 12 weeks.

Table 1: Adverse events with an incidence exceeding the placebo rate and reported by ≥1% of patients from double-blind, placebo-controlled Phase 3 trials of 12 weeks treatment duration

System organ class/Preferred term	Placebo N=554 %	Toviaz 4 mg/day N=554 %	Toviaz 8 mg/day N=566 %
Gastrointestinal disorders			
Dry mouth	7.0	18.8	34.6
Constipation	2.0	4.2	6.0
Dyspepsia	0.5	1.6	2.3
Nausea	1.3	0.7	1.9
Abdominal pain upper	0.5	1.1	0.5
Infections			
Urinary tract infection	3.1	3.2	4.2
Upper respiratory tract infection	2.2	2.5	1.8
Eye disorders			
Dry eyes	0	1.4	3.7
Renal and urinary disorders			
Dysuria	0.7	1.3	1.6
Urinary retention	0.2	1.1	1.4
Respiratory disorders			
Cough	0.5	1.6	0.9
Dry throat	0.4	0.9	2.3
General disorders			
Edema peripheral	0.7	0.7	1.2
Musculoskeletal disorders			
Back pain	0.4	2.0	0.9
Psychiatric disorders			
Insomnia	0.5	1.3	0.4
Investigations			
ALT increased	0.9	0.5	1.2
GGT increased	0.4	0.4	1.2
Skin disorders			
Rash	0.5	0.7	1.1

ALT = alanine aminotransferase; GGT = gamma glutamyltransferase

Patients also received Toviaz for up to three years in open-label extension phases of one Phase 2 and two Phase 3 controlled trials. In all open-label trials combined, 857, 701, 529, and 105 patients received Toviaz for at least 6 months, 1 year, 2 years, and 3 years, respectively. The adverse events observed during long-term, open-label studies were similar to those observed in the 12-week, placebo-controlled studies, and included dry mouth, constipation, dry eyes, dyspepsia, and abdominal pain. Similar to the controlled studies, most adverse events of dry mouth and constipation were mild to moderate in intensity. Serious adverse events, judged to be at least possibly related to study medication by the investigator and reported more than once during the open-label

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