Fair Balance & Web Link Destination Examples (HCP advertising)

July 2013

Guidance Document Content Flow

Purpose

This document is essentially a collection of examples. Its purpose is to crystalize the principles in PAAB codes 4.4 & 7.3 and the concepts discussed in the PAAB guidance documents "Guidance on generating the three base fair balance levels (HCP advertising)" and "Guidance on base fair balance level selection and placement in Healthcare Professional APS". It is strongly recommended that you read those documents prior to reading the present document.

The Old

Figure 1 shows the 2012 Toviaz journal ad while Figure 2 shows the PI that this ad refers to.

Figure 1: Layout for the 2012 Toviaz journal ad (i.e. before the code change).

The fair balance is in the bottom left quadrant. Additionally, the icon in the extreme bottom right corner directs the reader to go to page 76 within the publication for the prescribing summary. Figure 2 is the prescribing summary spanning over 2 pages. This is what the reader would see upon arrival to page 76.

Figure 2: Toviaz 2012 Prescribing Summary (2 pages)

Toviaz™
fesoterodine fumarate
extended-release tablets 4 mg and 8 mg

Prescribing Summary

Patient Selection Criteria

THERAPEUTIC CLASSIFICATION: Anticholinergic – Antispasmodic Agent

INDICATIONS AND CLINICAL USE: "TOVIAZ™ (fesoterodine fumarate extended-release tablet) is indicated for the treatment of patients with overactive bladder with symptoms of urinary frequency, urgency, or urge incontinence, or any combination of these symptoms. **Geriatrics (>65 years of age):** Based on clinical studies, no apparent overall differences were observed in safety between older (patients ≥65 years) and younger patients (patients <65 years) on fesoterodine extended-release tablets. Therefore, dosage adjustment for geriatric patients may not be required (see **SPECIAL POPULATIONS**). **Pediatrics (<18 years of age):** The safety and efficacy of **TOVIAZ** in pediatric populations have not been established.

CONTRAINDICATIONS: TOVIAZ is contraindicated in patients with: urinary retention, gastric retention, uncontrolled narrow-angle glaucoma, hypersensitivity to this drug, tolterodine L-tartrate tablets, tolterodine L-tartrate extended-release capsules, soya, peanuts, lactose, any of the other ingredients in the formulation or any component of the container.

SPECIAL POPULATIONS: Pregnant Women: There are no adequate data from the use of fesoterodine in pregnant women. Reproductive toxicity studies with fesoterodine in animals show embryotoxicity at doses close to maternally toxic ones. The potential risk for humans is unknown. Therefore, fesoterodine should be used during pregnancy only if the potential benefit to the mother outweighs the potential risk to the foetus. Women of childbearing potential should be considered for treatment only if using adequate contraception. **Nursing Women:** It is not known whether fesoterodine is excreted into human milk; therefore, breastfeeding is not recommended during treatment with fesoterodine. **Pediatrics (<18 years of age):** The safety and efficacy of **TOVIAZ** in pediatric patients have not been established. **Geriatrics (>65 years of age):** No overall differences in safety or effectiveness were observed between patients younger than 65 years of age and those 65 years of age or older in the clinical studies. However, patients in these studies were highly selected and relatively healthy. Dose-adjustment may not be required for the elderly. The pharmacokinetics of fesoterodine are not significantly influenced by age (see **ADVERSE REACTIONS** – Geriatrics).

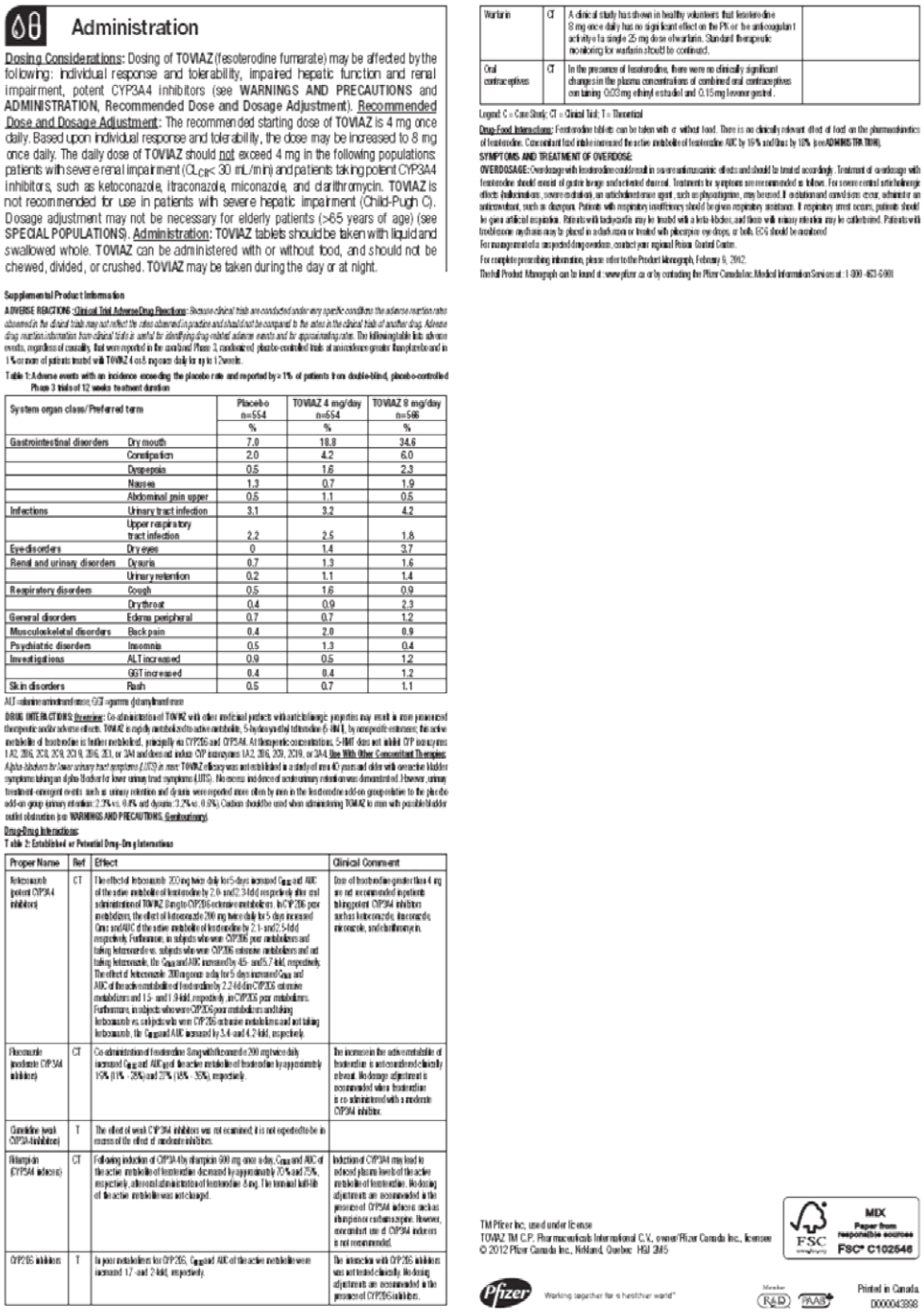
Safety Information

WARNINGS AND PRECAUTIONS: Cardiovascular: **TOVIAZ**, like other antimuscarinic drugs, is associated with increased heart rate that correlates with increasing dose. Accordingly, as with other antimuscarinic drugs, caution should be used when administering **TOVIAZ** to patients who have a history of ischemic heart disease or tachyarrhythmias. Endocrine/Metabolism: CYP3A4: Caution should be exercised when prescribing or up-titrating fesoterodine from 4 mg to 8 mg in patients in whom an increased exposure to the active metabolite is expected, such as with concomitant administration of CYP3A4 inhibitors. In the presence of a potent CYP3A4 inhibitor (e.g., ketaconazole, itraconazole, miconazole, and clarithromycin), doses of **TOVIAZ** greater than 4 mg are not recommended. In the presence of moderate CYP3A4 inhibitors (e.g., fluconazole), no dosing adjustments are recommended. While the effect of weak CYP3A4 inhibitors (e.g., cimetidine) was not examined in a clinical study, some pharmacokinetic interaction is expected, though less than what was observed with moderate CYP3A4 inhibitors (see **ADMINISTRATION** and **Supplemental Product Information**). CYP2D6: As subset of individuals are poor metabolizers for CYP2D6. Compared with CYP2D6 extensive metabolizers not taking ketoconazole (a potent CYP3A4 inhibitor), further increases in the exposure to the active metabolite of fesoterodine were observed in subjects who were CYP2D6 poor metabolizers taking ketoconazole (see **Supplemental Product Information**). Gastrointestinal: **Patients at Risk of Gastric Retention: TOVIAZ**, like other antimuscarinic drugs, should be administered with caution to patients with decreased gastrointestinal motility, including patients with severe constipation and to patients with gastrointestinal obstruction disorders (e.g., pyloric stenosis) because of the risk of gastric retention (see **CONTRAINDICATIONS**). Genitourinary: **Patients at Risk of Urinary Retention: TOVIAZ**, like other antimuscarinic drugs, should be administered with caution to patients with clinically significant bladder outlet obstruction because of the risk of urinary retention (see **CONTRAINDICATIONS** and **Supplemental Product Information**). Hepatic/Biliary/Pancreatic: **TOVIAZ** should be administered with caution to patients with impaired hepatic function. In patients with mild to moderate hepatic impairment, no dosage adjustment is required. Fesoterodine is not recommended for use in patients with severe hepatic impairment (see **ADMINISTRATION**). Immune: **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. Lactose: **TOVIAZ** extended-release tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactose deficiency or glucose-galactose malabsorption should not take this medicinal product. Neurologic: **TOVIAZ**, like other antimuscarinic drugs, should be administered with caution to patients with myasthenia gravis. Ophthalmologic: **Controlled Narrow-Angle Glaucoma: TOVIAZ**, like other antimuscarinic drugs, should be used with caution in patients being treated for narrow-angle glaucoma (see **CONTRAINDICATIONS**). Renal: **TOVIAZ** should be administered with caution to patients with impaired renal function. In patients with mild-to-moderate renal impairment, no dosage adjustment is required. Doses of fesoterodine greater than 4 mg are not recommended in patients with severe renal impairment (CL_{CR}<30 mL/min) (see **ADMINISTRATION**).

ADVERSE REACTION (see full listing): Adverse Drug Reaction Overview: Due to the pharmacological properties of fesoterodine, treatment may cause mild-to-moderate antimuscarinic effects like dry mouth, constipation, dry eyes, and dyspepsia. Clinical Trial Adverse Drug Reactions: The safety of **TOVIAZ** was primarily 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**. A total of 1964 patients participated in two 12-week, Phase 3 efficacy and safety studies and subsequent open-label extension studies. In these 2 studies combined, 564 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 **TOVIAZ** 4 mg/day, and 6% in those taking **TOVIAZ** 8 mg. 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 treatment period of up to 3 years included urinary retention (3 cases), diverticulitis (3 cases), constipation (2 cases), irritable bowel syndrome (2 cases), and electrocardiogram QT corrected interval prolongation (2 cases). The safety of **TOVIAZ** was further established in two additional 12-week, active- and placebo-controlled, double-blind, randomized studies comparing **TOVIAZ** with tolterodine ER 4 mg and placebo. In these studies combined, 1527 patients received **TOVIAZ** 8 mg, 1552 patients received tolterodine ER 4 mg, and 755 patients received placebo. The most common treatment-emergent adverse events (dry mouth, constipation, and headache) reported with **TOVIAZ** during these 2 studies were similar to those observed in the 12-week, placebo-controlled studies. In clinical trials comparing fesoterodine to placebo, cases of markedly elevated liver enzymes (ALT increased, GGT increased) were reported at a frequency no different than placebo. The relation to fesoterodine treatment is unclear. **TOVIAZ** was associated with an increase in heart rate that correlated with increasing dose, a well-characterized effect described for antimuscarinic drugs. In the placebo-controlled phase 3 studies in patients with overactive bladder, the mean increases in heart rate compared to placebo were approximately 3-4 beats/minute in the 4 mg/day group and 3-5 beats/minute in the 8 mg/day group. **Geriatrics (>65 years of age):** Of 1567 patients who received **TOVIAZ** 4 mg/day or 8 mg/day in the Phase 2 and 3, placebo-controlled, efficacy and safety studies, 515 (33%) were 65 years of age or older, and 140 (9%) were 75 years of age or older. No overall differences in safety or efficacy were observed between patients younger than 65 years of age and those 65 years of age or older in these studies; however, the incidence of antimuscarinic adverse events, including dry mouth, constipation, dyspepsia, increase in residual urine, dizziness (at 8 mg only) and urinary tract infection, was higher in patients 75 years of age and older as compared to younger patients. Post-Market Adverse Drug Reactions: The following events have been reported in association with fesoterodine use in worldwide post-marketing experience: *Eye disorders*: Blurred vision; *Cardiac disorders*: Palpitations; *Skin and subcutaneous tissue disorders*: Angioedema including angioedema with airway obstruction, face edema, hypersensitivity reactions; *Renal and urinary disorders*: Urinary retention. Because these spontaneously reported events are from the worldwide post-marketing experience, the frequency of the events and the role of fesoterodine in their causation cannot be reliably determined.

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
  - Fax toll-free to 1-866-678-6789, or
  - Mail to: Canada Vigilance Program, Health Canada
    Postal Locator 0701C, Ottawa, ON K1A 0K9



Administration

Dosing Considerations: Dosing of TOVIAZ (fesoterodine fumarate) may be affected by the following: individual response and tolerability, impaired hepatic function and renal impairment, potent CYP3A4 inhibitors (see WARNINGS AND PRECAUTIONS and ADMINISTRATION, Recommended Dose and Dosage Adjustment). **Recommended Dose and Dosage Adjustment:** 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) and patients taking potent CYP3A4 inhibitors, such as ketoconazole, itraconazole, miconazole, and clarithromycin. TOVIAZ is not recommended for use in patients with severe hepatic impairment (Child-Pugh C). Dosage adjustment may not be necessary for elderly patients (≥65 years of age) (see SPECIAL POPULATIONS). **Administration:** TOVIAZ tablets should be taken with liquid and swallowed whole. TOVIAZ can be administered with or without food, and should not be chewed, divided, or crushed. TOVIAZ may be taken during the day or at night.

Supplemental Product Information

ADVERSE REACTIONS: Clinical Trial Adverse Drug Reactions: *Because clinical trials are conducted under very specific conditions the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse drug reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.* The following table 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

DRUG INTERACTIONS: Overview: Co-administration of TOVIAZ with other medicinal products with anticholinergic properties may result in more pronounced therapeutic and/or adverse effects. TOVIAZ is rapidly metabolized to active metabolite, 5-hydroxymethyl tolterodine (5-HM), by nonspecific esterases; the active metabolite of fesoterodine is further metabolized, principally via CYP2D6 and CYP3A4. At therapeutic concentrations, 5-HM does not inhibit CYP isoenzymes 1A2, 2B6, 2C8, 2C9, 2C19, 2D6, 2E1, or 3A4 and does not induce CYP isoenzymes 1A2, 2B6, 2C9, 2C19, or 3A4. **Use With Other Concomitant Therapies:** *Alpha-blockers for lower urinary tract symptoms (LUTS) in men:* TOVIAZ efficacy was not established in a study of men 40 years and older with overactive bladder symptoms taking an alpha-blocker for lower urinary tract symptoms (LUTS). No excess incidence of acute urinary retention was demonstrated. However, urinary treatment-emergent events such as urinary retention and dysuria were reported more often by men in the fesoterodine add-on groups relative to the placebo add-on group: urinary retention: 2.7% vs. 0.4% and dysuria: 3.2% vs. 0.8%). Caution should be used when administering TOVIAZ to men with possible bladder outlet obstruction (see WARNINGS AND PRECAUTIONS, Genitourinary).

Drug-Drug Interactions:

Table 2: Established or Potential Drug-Drug Interactions

Proper Name	Ref	Effect	Clinical Comment
Ketoconazole (potent CYP3A4 inhibitor)	CT	The effect of ketoconazole 200 mg twice daily for 5 days increased C_{max} and AUC of the active metabolite of fesoterodine by 2.0- and 2.3-fold respectively after oral administration of TOVIAZ 8 mg to CYP2D6 extensive metabolizers. In CYP2D6 poor metabolizers, the effect of ketoconazole 200 mg twice daily for 5 days increased C_{max} and AUC of the active metabolite of fesoterodine by 2.1- and 2.5-fold respectively. Furthermore, in subjects who were CYP2D6 poor metabolizers and taking ketoconazole vs. subjects who were CYP2D6 extensive metabolizers and not taking ketoconazole, the C_{max} and AUC increased by 4.5- and 5.7-fold, respectively. The effect of ketoconazole 200 mg once daily for 5 days increased C_{max} and AUC of the active metabolite of fesoterodine by 2.2-fold in CYP2D6 extensive metabolizers and 1.5- and 1.9-fold, respectively, in CYP2D6 poor metabolizers. Furthermore, in subjects who were CYP2D6 poor metabolizers and taking ketoconazole vs. subjects who were CYP2D6 extensive metabolizers and not taking ketoconazole, the C_{max} and AUC increased by 3.4- and 4.2-fold, respectively.	Dose of fesoterodine greater than 4 mg are not recommended in patients taking potent CYP3A4 inhibitors such as ketoconazole, itraconazole, miconazole, and clarithromycin.
Fluconazole (moderate CYP3A4 inhibitor)	CT	Co-administration of fesoterodine 8 mg with fluconazole 200 mg twice daily increased C_{max} and AUC of the active metabolite of fesoterodine by approximately 19% (11% - 28%) and 27% (18% - 35%), respectively.	The increase in the active metabolite of fesoterodine is not considered clinically relevant. No dosage adjustment is recommended when fesoterodine is co-administered with a moderate CYP3A4 inhibitor.
Cimetidine (weak CYP3A inhibitor)	T	The effect of weak CYP3A4 inhibitors was not examined, it is not expected to be in excess of the effect of moderate inhibitors.	
Rifampin (CYP3A4 inducer)	CT	Following induction of CYP3A4 by rifampin 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. The terminal half-life of the active metabolite was unchanged.	Induction of CYP3A4 may lead to reduced plasma levels of the active metabolite of fesoterodine. No dosing adjustments are recommended in the presence of CYP3A4 inducers such as rifampicin or carbamazepine. However, concomitant use of CYP3A4 inducers is not recommended.
CYP2D6 inhibitors	T	In poor metabolizers for CYP2D6, C_{max} and AUC of the active metabolite were increased 1.7- and 2-fold, respectively.	The interaction with CYP2D6 inhibitors was not tested clinically. No dosing adjustments are recommended in the presence of CYP2D6 inhibitors.
Warfarin	CT	A clinical study has shown in healthy volunteers that fesoterodine 8 mg once daily has no significant effect on the PK or the anticoagulant activity of a single 25 mg dose of warfarin. Standard therapeutic monitoring for warfarin should be continued.	
Oral contraceptives	CT	In the presence of fesoterodine, there were no clinically significant changes in the plasma concentrations of combined oral contraceptives containing 0.03 mg ethinyl estradiol and 0.15 mg levonorgestrel.	

Legend: C = Case Study; CT = Clinical Trial; T = Theoretical

Drug-Food Interactions: Fesoterodine tablets can be taken with or without food. There is no clinically relevant effect of food on the pharmacokinetics of fesoterodine. Concomitant food intake increased the active metabolite of fesoterodine AUC by 16% and thus by 10% (see **ADMINISTRATION**).

SYMPTOMS AND TREATMENT OF OVERDOSE:

OVERDOSAGE: Overdosage with fesoterodine could result in severe antimuscarinic effects and should be treated accordingly. Treatment of overdosage with fesoterodine should consist of gastric lavage and activated charcoal. Treatments for symptoms are recommended as follows. For severe central anticholinergic effects (hallucinations, severe excitation), an anticholinesterase agent, such as physostigmine, may be used. If excitation and convulsions occur, administer an anticonvulsant, such as diazepam. Patients with respiratory insufficiency should be given respiratory assistance. If respiratory arrest occurs, patients should be given artificial respiration. Patients with tachycardia may be treated with a beta-blocker, and those with urinary retention may be catheterized. Patients with trachycardia mechanism may be placed in a dark area or treated with physostigmine eye drops, or both. ECG should be monitored.

For management of a suspected drug overdose, contact your regional Poison Control Centre.

For complete prescribing information, please refer to the Product Monograph, February 6, 2012.

The full Product Monograph can be found at www.pfizer.ca or by contacting the Pfizer Canada Inc. Medical Information Services at: 1-800-463-6001

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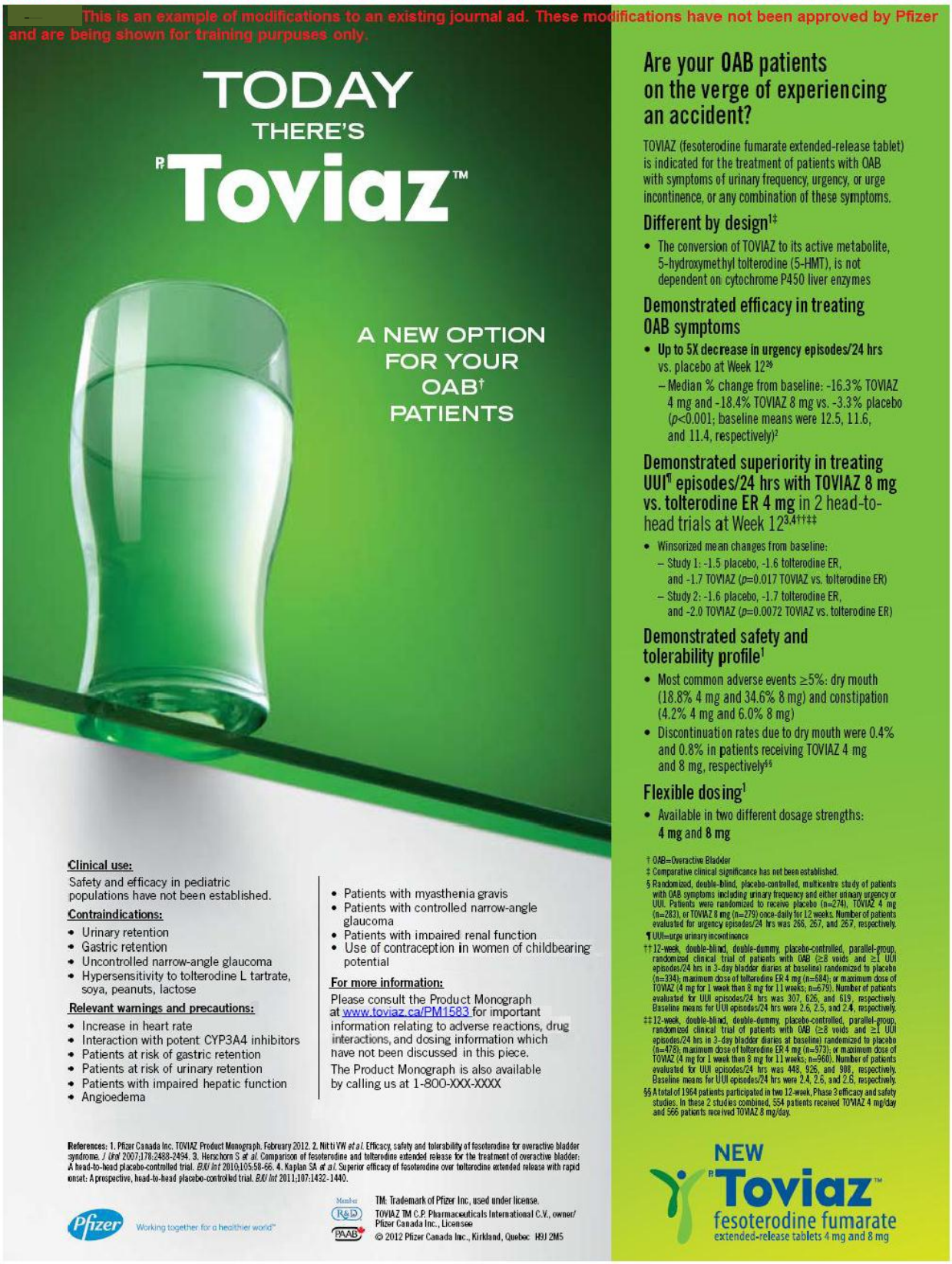
The New

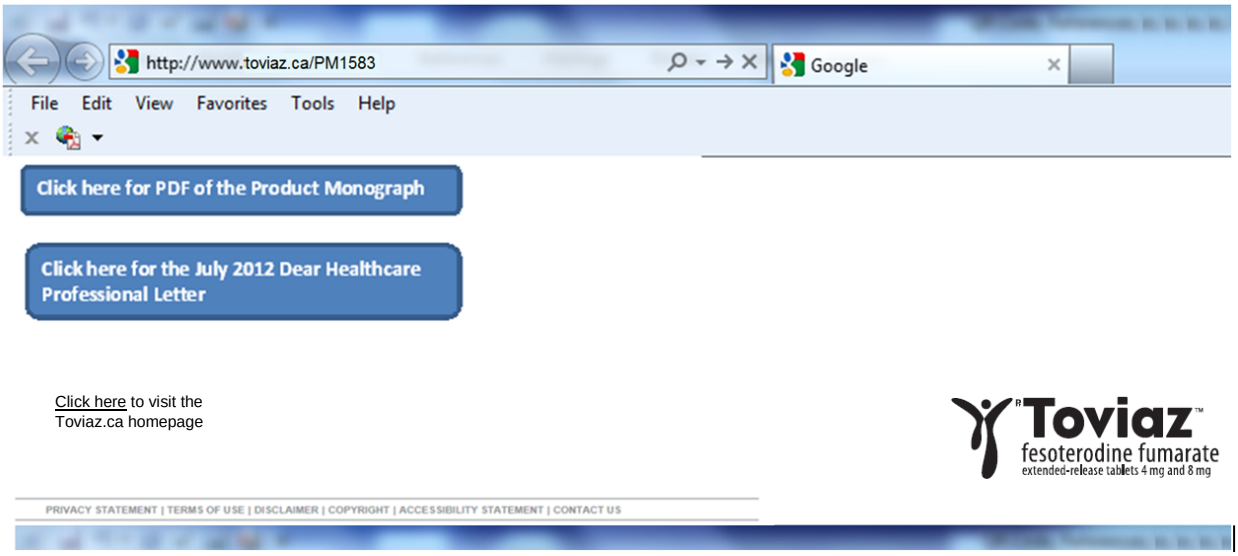
Figure 3 is one of the ways the Toviaz ad can look after the July 2013 PAAB code change. The highest level of base fair balance is employed because the APS contains therapeutic claims.

Figure 3: Toviaz highest level fair balance



The web page at URL www.toviaz.ca/PM1583 in the Figure 3 fair balance is a hypothetical page on the HCP gated website www.toviaz.ca. Figure 4 shows an example of what this hypothetical web page could look like (for training purposes only, this webpage does not exist and has not been approved by Pfizer). Note that Toviaz does not have a July 2012 Dear HCP letter. The corresponding icon has been added for demonstration purposes only.

Figure 4: Hypothetical web link destination for Toviaz

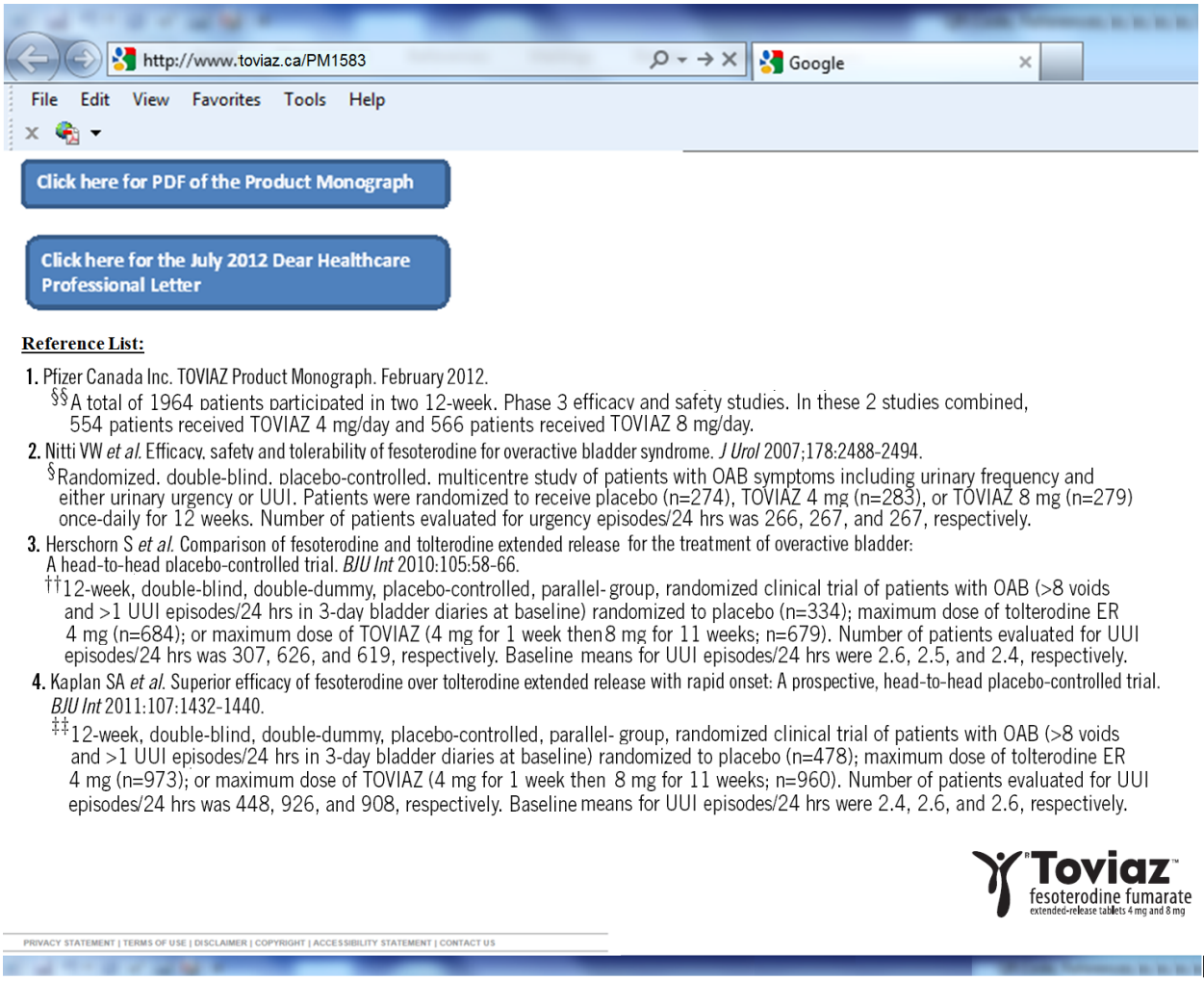


As per PAAB code section 7.3, this page must be accessible without the need to enter a password. This is possible as the APS containing the URL is distributed or made viewable in controlled fashion (i.e. targeted for HCPs). The URL itself therefore acts as the key into the Toviaz website. This is why you'll note the URL is not simply www.toviaz.ca. There is no need for PAAB review of this web page provided the content is limited to that listed in PAAB code section 7.3.2b. The references and study parameters are reviewed within the context of the corresponding APS.

The reference list and the study parameters may appear in APS as in Figure 3. However, they could have alternatively been moved to the web link destination as shown in Figure 5. The click through to the TMA (and the Dear HCP letter if applicable) must be **very** prominent on the web link destination (e.g. large and the first item on the page).

Please note that the study parameters and the reference list may appear either on the face of the weblink destination (as in Figure 5) or they may be relegated to a click through button.

Figure 5: Hypothetical web link destination for Toviaz (with references & study parameters)



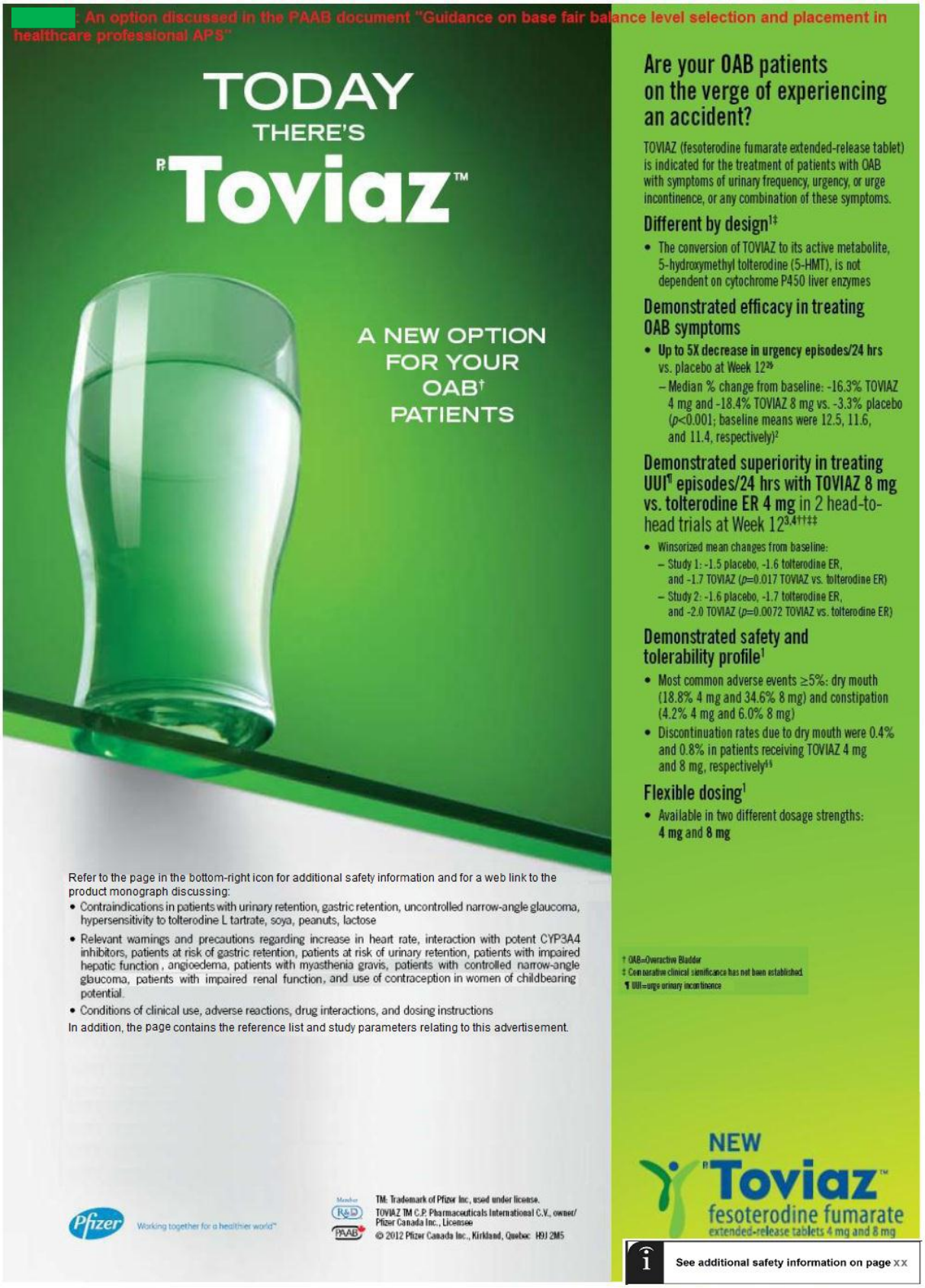
It is important to note that study parameters are the only footnotes which can be relegated to the web link destination. Disclaimers and definitions, for example, must remain on the face of the ad (on the same surface as the claims they are qualifying) in order to satisfy PAAB code section 2.1.

Rather than the Toviaz website, the manufacturer could have used a URL leading directly to the product monograph PDF document stored on the corporate website or to the Drug Product Directory search page on the Health Canada website. This would impose some limitations on the manufacturer options vis-à-vis the reference list and study parameters.

Using middle level to lead to highest level fair balance

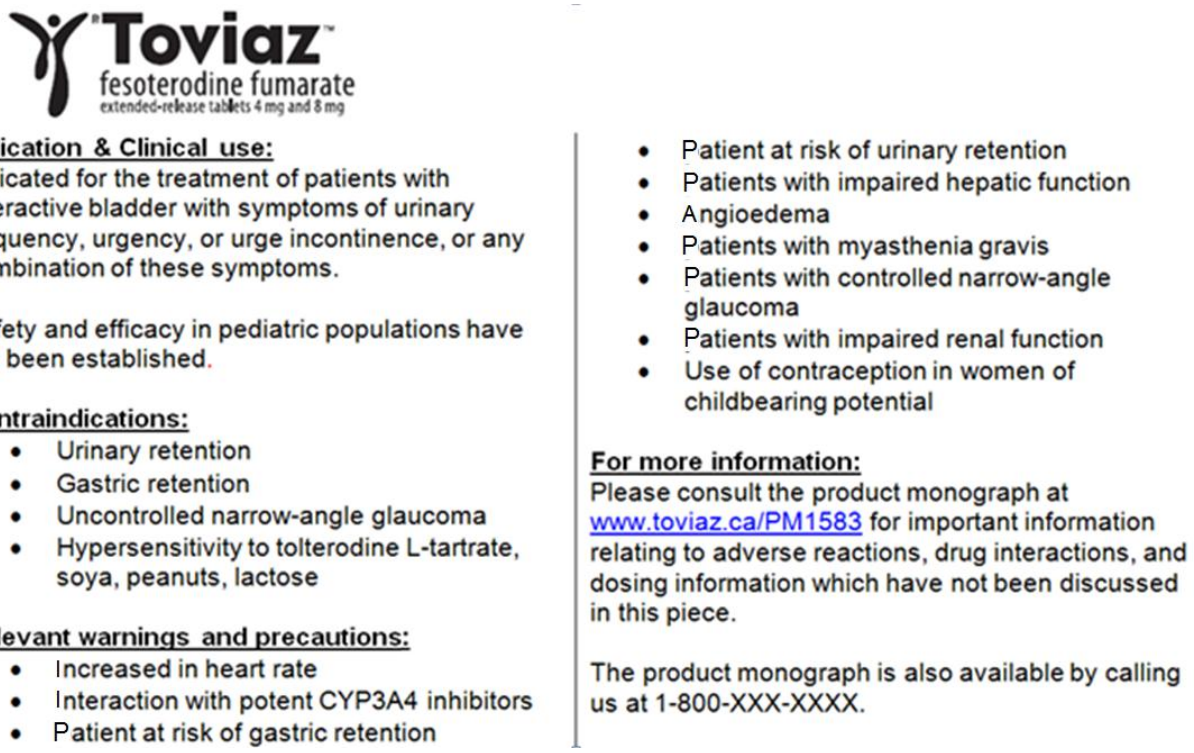
The APS in figure 3 employs the highest level fair balance as it has therapeutic claims. However, the manufacturer could instead choose to use middle fair balance on the face of the APS to direct the reader elsewhere to a surface which is easily accessible (e.g. same media) and conducive to easy reading. In Figure 6, we've modified the Figure 3 APS to accomplish this.

Figure 6: Middle level used to direct the reader to highest level fair balance



When the reader goes to page XX, they'll see Figure 7. In this case, www.toviaz.ca/PM1583 would be figure 5. Note that the relevant page XX presentation should begin with the product logo so as to be easily located (and differentiated from other content on the page).
As Toviaz does not have any emphasized warnings and precautions (e.g. bolded/boxed) or a long list of clinical use issues in the "Indication and Clinical Use" section of the product monograph, the benefits of using middle fair balance within the main advertising message to direct HCPs to the highest level elsewhere are not as pronounced as they would be for other products.

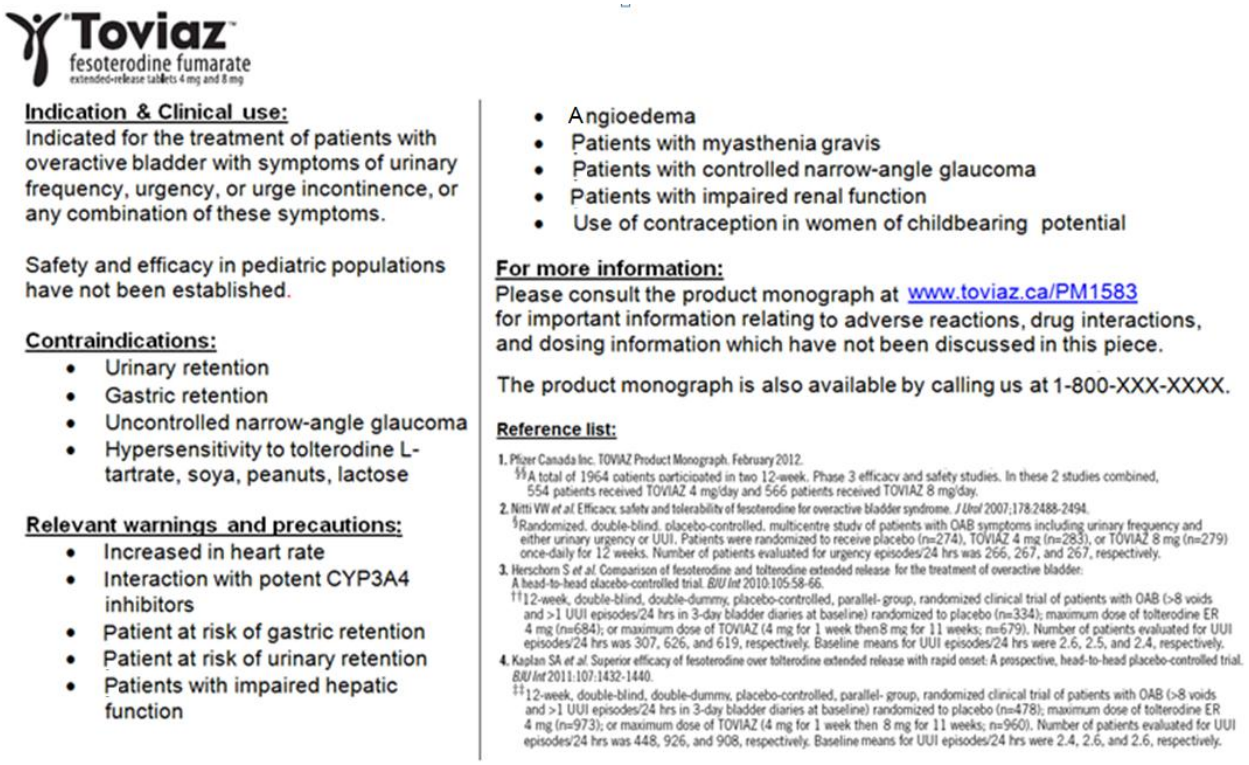
Figure 7: Highest fair balance placed elsewhere



This brings us to another potential location for references and study parameters. In Figure 8, we've added the references and study parameters to the surface containing the highest level fair balance (rather than keeping them on the ad or moving them to the web-link destination). In this case, www.toviaz.ca/PM1583 would be figure 4.

Figure 9 shows the minimum font sizes for content which does not appear on the face of the ad. These minimum requirements apply whether the content appears on the web link destination or elsewhere such as some other page within the publication. There are no minimum fair balance font sizes for content on the face of the ad (as fair balance size on the face of the ad should be comparable to the benefit copy font size).

Figure 8: Highest fair balance placed elsewhere with references and parameters



Toviaz
fesoterodine fumarate
extended-release tablets 4 mg and 8 mg

Indication & Clinical use:
Indicated for the treatment of patients with overactive bladder with symptoms of urinary frequency, urgency, or urge incontinence, or any combination of these symptoms.

Safety and efficacy in pediatric populations have not been established.

Contraindications:
- Urinary retention
- Gastric retention
- Uncontrolled narrow-angle glaucoma
- Hypersensitivity to tolterodine L-tartrate, soya, peanuts, lactose

Relevant warnings and precautions:
- Increased in heart rate
- Interaction with potent CYP3A4 inhibitors
- Patient at risk of gastric retention
- Patient at risk of urinary retention
- Patients with impaired hepatic function
- Angioedema
- Patients with myasthenia gravis
- Patients with controlled narrow-angle glaucoma
- Patients with impaired renal function
- Use of contraception in women of childbearing potential

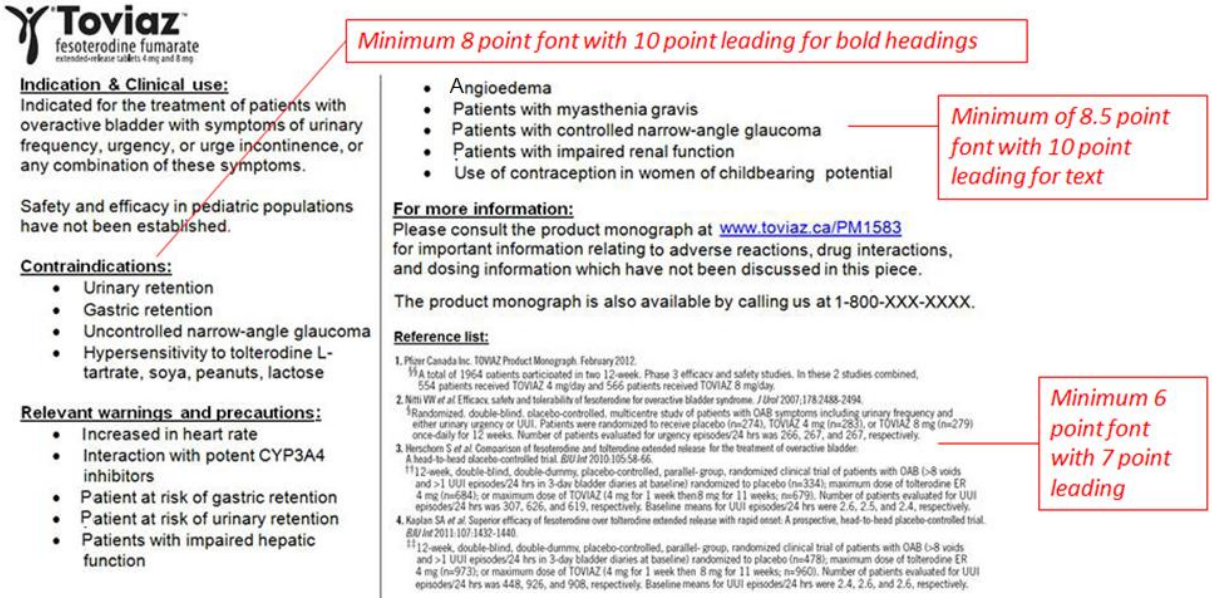
For more information:
Please consult the product monograph at www.toviaz.ca/PM1583 for important information relating to adverse reactions, drug interactions, and dosing information which have not been discussed in this piece.

The product monograph is also available by calling us at 1-800-XXX-XXXX.

Reference list:

1. Pfizer Canada Inc. TOVIAZ Product Monograph. February 2012.
   ††A total of 1964 patients participated in two 12-week. Phase 3 efficacy and safety studies. In these 2 studies combined, 554 patients received TOVIAZ 4 mg/day and 566 patients received TOVIAZ 8 mg/day.
2. Nitti VW *et al.* Efficacy, safety and tolerability of fesoterodine for overactive bladder syndrome. *J Urol* 2007;178:2488-2494.
   †Randomized, double-blind, placebo-controlled, multicentre study of patients with OAB symptoms including urinary frequency and either urinary urgency or UUI. Patients were randomized to receive placebo (n=274), TOVIAZ 4 mg (n=283), or TOVIAZ 8 mg (n=279) once-daily for 12 weeks. Number of patients evaluated for urgency episodes/24 hrs was 266, 267, and 267, respectively.
3. Herschorn S *et al.* Comparison of fesoterodine and tolterodine extended release for the treatment of overactive bladder: A head-to-head placebo-controlled trial. *BJU Int* 2010;105:58-66.
   ††12-week, double-blind, double-dummy, placebo-controlled, parallel- group, randomized clinical trial of patients with OAB (>8 voids and >1 UUI episodes/24 hrs in 3-day bladder diaries at baseline) randomized to placebo (n=334); maximum dose of tolterodine ER 4 mg (n=684); or maximum dose of TOVIAZ (4 mg for 1 week then 8 mg for 11 weeks; n=679). Number of patients evaluated for UUI episodes/24 hrs was 307, 626, and 619, respectively. Baseline means for UUI episodes/24 hrs were 2.6, 2.5, and 2.4, respectively.
4. Kaplan SA *et al.* Superior efficacy of fesoterodine over tolterodine extended release with rapid onset: A prospective, head-to-head placebo-controlled trial. *BJU Int* 2011;107:1432-1440.
   ‡‡12-week, double-blind, double-dummy, placebo-controlled, parallel- group, randomized clinical trial of patients with OAB (>8 voids and >1 UUI episodes/24 hrs in 3-day bladder diaries at baseline) randomized to placebo (n=478); maximum dose of tolterodine ER 4 mg (n=973); or maximum dose of TOVIAZ (4 mg for 1 week then 8 mg for 11 weeks; n=960). Number of patients evaluated for UUI episodes/24 hrs was 448, 926, and 908, respectively. Baseline means for UUI episodes/24 hrs were 2.4, 2.6, and 2.6, respectively.

Figure 9: Font sizes for content which is **not** located on the face of the ad



Toviaz
fesoterodine fumarate
extended-release tablets 4 mg and 8 mg

Indication & Clinical use:
Indicated for the treatment of patients with overactive bladder with symptoms of urinary frequency, urgency, or urge incontinence, or any combination of these symptoms.

Safety and efficacy in pediatric populations have not been established.

Contraindications:
- Urinary retention
- Gastric retention
- Uncontrolled narrow-angle glaucoma
- Hypersensitivity to tolterodine L-tartrate, soya, peanuts, lactose

Relevant warnings and precautions:
- Increased in heart rate
- Interaction with potent CYP3A4 inhibitors
- Patient at risk of gastric retention
- Patient at risk of urinary retention
- Patients with impaired hepatic function
- Angioedema
- Patients with myasthenia gravis
- Patients with controlled narrow-angle glaucoma
- Patients with impaired renal function
- Use of contraception in women of childbearing potential

For more information:
Please consult the product monograph at www.toviaz.ca/PM1583 for important information relating to adverse reactions, drug interactions, and dosing information which have not been discussed in this piece.

The product monograph is also available by calling us at 1-800-XXX-XXXX.

Reference list:

1. Pfizer Canada Inc. TOVIAZ Product Monograph. February 2012.
   ††A total of 1964 patients participated in two 12-week. Phase 3 efficacy and safety studies. In these 2 studies combined, 554 patients received TOVIAZ 4 mg/day and 566 patients received TOVIAZ 8 mg/day.
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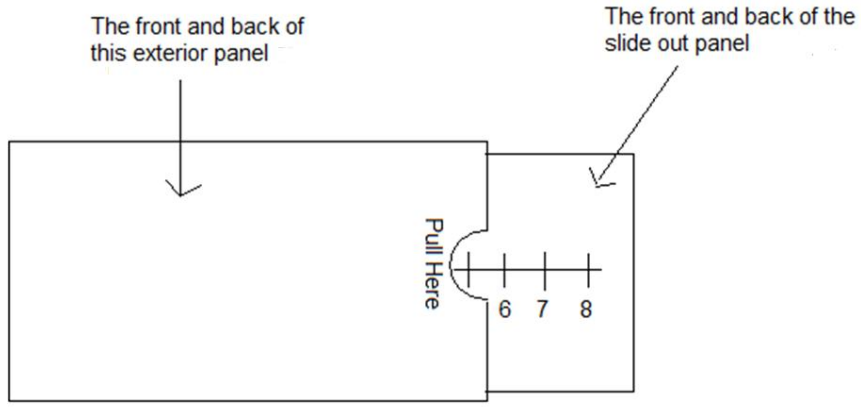
Other key uses for middle level leading to highest level fair balance

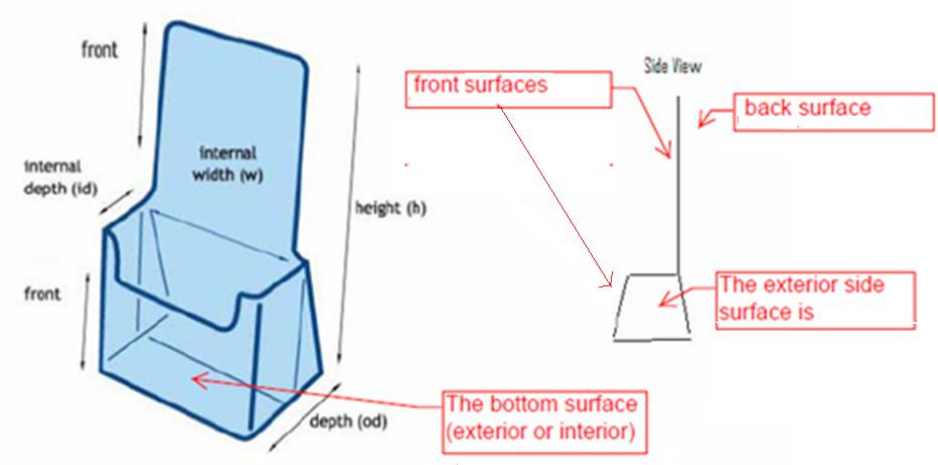
For a slide ruler (see figure 10) the main advertising area is generally confined to the external outer facing surfaces (front & back). The ruler itself, which slides out, is not considered part of the main advertising surface. The manufacturer has the option of placing middle level fair balance on the exterior directing the reader to remove the ruler in order to access the highest level fair balance. It is possible that the ruler even unfolds thus offering a larger surface area. The reader then folds the ruler and easily slides it back into the outer case for continued use of the tool.
Other tools like bellybands, shelf talkers and tent cards offer similar opportunities.

Figure 10: Slide ruler



The main advertising area on a sample holder (see figure 11) is generally confined to the front-facing and side-facing panels. The back panel is typically pushed up against the back of the cupboard wall. Middle level fair balance can be used on the front or side panels to direct the HCP to pull the holder out of the cupboard so as to view the back panel for the highest level fair balance. Note that the highest level fair balance may not appear on the inside panels or the bottom panel as reading content on these surfaces would require awkward positioning or emptying of the sample tray. For similar reasons, the highest level of fair balance could not appear on the top or bottom shelf talker surfaces which rest on the shelf (i.e. product would need to be removed to make the balance copy visible).

Figure 11: Sample holder



Electronic banner ads in HCP gated environments which contain product claims require fair balance. Relegating the fair balance to a click through would not meet this requirement as this would constitute separation of the claims from the fair balance. However, middle fair balance may appear on the face of the banner with a click through directly to the highest fair balance. In such a case, the highest fair balance should be presented on the face of the weblink destination (i.e. the highest level fair balance should not be relegated to a button found on the weblink destination requiring additional click through). Although this disqualifies the weblink destination from being exempt from preclearance, this option simplifies communication of therapeutic claims on banner ads. Note that where multiple frames are used in the banner ad, the indication should appear on (or prior to) the first frame containing explicit marketing claims of benefit (refer to the document "Guidance on Indication Placement in Advertising").

Please refer to the PAAB document "Guidance on base fair balance level selection and placement" for discussion on the use of middle fair balance on the homepage of product websites.

The Web Link Destination

The URL or electronic link can lead to any of the destination pages listed in PAAB code section 7.3.

Web link destinations on company/agent controlled product or corporate websites containing content which exceed the elements listed in 7.3.2b require PAAB review as a separate APS. All visible content on such pages (including but not limited to links and/or menu items) would be reviewed in the product branded context.