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PROPRIETARY DRUG NAME® / GENERIC DRUG NAME: Toviaz® / Fesoterodine Fumarate

PROTOCOL NO.: A0221090

PROTOCOL TITLE: A Local, Multicentre, Open-Label, Extension Trial to Evaluate the Efficacy and Safety of Fesoterodine Flexible Dose Regimen in Elderly Patients With Overactive Bladder

Study Centers: Four centers in Portugal took part in the study and enrolled subjects.

Study Initiation Date and Final Completion Date: 25 May 2010 to 04 January 2012

Phase of Development: Phase 4

Study Objectives:

Primary Objective:

- To assess the long-term efficacy, in terms of maintenance of fesoterodine effect on urgency episode frequency in elderly subjects with overactive bladder (OAB).

Secondary Objectives:

- To assess the long-term safety and tolerability of fesoterodine in elderly subjects with OAB;

- To assess the long-term efficacy, in terms of maintenance of fesoterodine effect on other OAB symptoms, and on subject reported outcomes, in elderly subjects with OAB.

METHODS

Study Design: This was a local, multicenter, open-label, extension study, intended for elderly subjects (≥65 years) with OAB who had completed treatment in previous fesoterodine study (Study A0221045: a 24-week, multicenter trial, comprising a 12-week, randomized, double-blind, placebo-controlled, parallel-group phase followed by a 12-week open-label phase, to evaluate the efficacy and safety of a fesoterodine flexible dose regimen in elderly patients with OAB [NCT00798434]). This study consisted of an enrollment visit after the subject's completion of previous fesoterodine study, followed by visits every 3 months, and an end-of-treatment (EOT) visit, which was performed when the study ended (31 December 2011), or if the subject withdrew (whichever was earlier). Subjects were

treated according to the regimen received in previous fesoterodine study and the Investigator's evaluation. Table 1 presents the schedule of activities in the study.

Table 1. Schedule of Activities

Protocol Activity	Enrollment[a]	Every 3 Months (M3, M6, M9)[b] (±2 Weeks)	End-of-Treatment or Early Termination/ Withdrawal[c]	SAE Follow Up (+2 Weeks After Onset of the SAE)
Informed consent	X			
Demographics & medical history	X			
Sitting BP & pulse rate	X	X	X	
Physical examination	X			
Dispense micturition bladder diary (3-day)	X	X		
Evaluation of micturition bladder diary (3-day)		X	X	
KHQ	X		X	
PPBC	X	X	X	
PPUS	X	X	X	
OAB-q	X	X	X	
OAB-s	X	X	X	
AEs	X	X	X	X
Concomitant medication and nondrug treatment	X	X	X	
Dispense study medication[d]	X	X		
Study medication return/count		X	X	
Assess drug compliance		X	X	

AE = adverse event; BP = blood pressure; EOT = end-of-treatment; KHQ = King's Health Questionnaire; OAB-q = Overactive Bladder Questionnaire; OAB-s = Overactive Bladder Satisfaction Questionnaire; PPBC = Patient Perception of Bladder Condition; PPUS = Patient Perception of Urgency Scale; SAE = serious adverse event.

a. Subjects completed the Week 24 procedures from previous fesoterodine study in addition to the activities for this study.
b. After this study enrollment visit.
c. EOT visit occurred when the subject switched to commercial fesoterodine, when the study ended (31 December 2011), or when the subject withdrew (whichever was earliest).
d. Treatment assignments in the this study extension study were carried forward from the prior assignment in previous fesoterodine study

Number of Subjects (Planned and Analyzed): The number of subjects to be enrolled was not based on statistical considerations but rather was dependent upon the number of subjects who completed the previous fesoterodine study from sites in Portugal and who elected to continue with this extension study. From the subjects based in Portugal who participated in the parent study (N=63), approximately 26 subjects were planned to be included in this extension study.

A total of 31 subjects (49% of subjects who participated in the parent study in Portugal) were screened for inclusion in this study; all subjects received at least 1 dose of study drug.

Diagnosis and Main Criteria for Inclusion: Both males and females of age 65 years or older who had completed the previous fesoterodine study (in Portugal) and were recommended for inclusion by the Investigator.

Study Treatment: Eligible subjects received either 4 or 8 mg fesoterodine according to the previous regime received in the previous fesoterodine study and the Investigator's evaluation. The subjects were instructed to take the study drug in the morning (within 2 hours of rising)

or in the evening (within 4 hours prior to bedtime). Tablets were to be swallowed whole with water, and could have been taken with or without food.

Efficacy and Safety Endpoints:

Efficacy Endpoints:

Primary Endpoint: The mean number of micturition related urgency episodes per 24 hours at EOT. Micturition-related urgency episodes were defined as those with Urinary Sensation Scale (USS) rating of ≥3 marked for the corresponding micturition in the diary.

Secondary Endpoints: Secondary efficacy endpoints were assessed with the help of micturition diary and by use of questionnaires.

- Mean number of micturition-related urgency episodes per 24 hours at each visit (urgency episodes were defined as those with the USS rating of ≥3 in the diary);
- Mean number of severe micturition-related urgency episodes per 24 hours at each visit (severe urgency episodes were defined as those with the USS rating ≥4);
- Mean number of micturitions per 24 hours at each visit (micturitions include episodes of voluntary micturition and episodes of urgency urinary incontinence [UUI]);
- Mean number of night-time micturitions per 24 hours at each visit. Night-time micturitions per 24 hours were those occurring after 'time to bed' and before 'time arose' in the next day;
- Mean number of UUI episodes per 24 hours at each visit (UUI episodes were defined as those with the USS rating of 5 in the diary);
- Daily sum rating in the USS at each visit. The sum rating per 24 hours was calculated as the mean rating scores on the Bladder Sensation Scale multiplied by the mean number of micturitions per 24 hours at that visit;
- The percentage of subjects who were incontinent at enrollment visit (at least 1 UUI episode during the enrollment visit period) and were dry (no UUI episodes) in the 3 days prior to each visit. UUI episodes were defined as those with the USS rating of 5 in the diary;
- Number of urinary incontinence pads, barrier creams and powder (for skin protection) used by subjects with UUI.

Subject Questionnaires: The following questionnaires were used in the study:

- Patient Perception of Bladder Condition (PPBC) (1 question);
- Patient Perception of Urgency Scale (PPUS) (1 question);

- Overactive Bladder Questionnaire (OAB-q) (33 questions);
    - Total score of OAB-q at each visit;
    - Total score of each domain of OAB-q at each visit;
- Overactive Bladder Satisfaction Questionnaire (OAB-s) (4 questions);
    - Scores from the selected items at each visit;
- King's Health Questionnaire (KHQ) (21 questions; used to compare the performance of the KHQ with the other QOL instruments);
    - Total score of each domain of KHQ at each visit.

Safety Endpoints: Safety evaluations included adverse events (AEs), concomitant drug and nondrug treatments, drug compliance, and vital signs measurements. Medical history and physical examinations were performed at enrollment only.

Safety Evaluations: AEs, concomitant drug and nondrug treatments, and vital signs measurements, medical history and physical examinations were performed at specified time (Table 1) during the study.

Statistical Methods:

Full Analysis Set (FAS): The FAS consisted of all subjects who were enrolled in the study, took at least 1 dose of study treatment during the study, and completed at least 1 micturition diary (in addition to enrollment).

Safety Analysis Set: The safety population consisted of all subjects who took at least 1 dose of study medication.

Efficacy analysis was based on the FAS. The primary endpoint, the mean number of micturition-related urgency episodes per 24 hours at EOT, was summarized at each visit using descriptive statistics.

All diary-derived endpoints were summarized for number of subjects, mean (95% confidence interval [CI] for mean), median, standard deviation (SD), minimum, and maximum. The percentage of subjects who were incontinent at enrollment and were dry (no UUI episodes) in the 3 days prior to each visit were summarized as categorical variables at each visit. Incontinent at the enrollment visit was defined as at least 1 UUI episode during the enrollment visit period, and for the purposes of this analysis, this was defined as the baseline diary from previous fesoterodine study.

Patient Perception of Bladder Condition and Patient Perception of Urgency Scale: Categorical responses to the PPBC and PPUS questionnaires were summarized for counts and percentage using frequency tables for each visit. The change from enrollment categories

("Deterioration," "No Change," and "Improvement") were also summarized as categorical variables for both PPBC and PPUS at each post-enrollment visit.

Overactive Bladder Questionnaire: The total score and domains score were summarized for each visit using number of subjects, mean (and 95% CI for the mean), median, SD, minimum, and maximum.

Overactive Bladder Satisfaction Questionnaire: Frequency tables (counts and percentages in each response category) for each visit were presented. Respondents from Questions 5, 9, 10a-10d, and 11a-11b for each visit were summarized as categorical variables. The total score (calculated from scores in Questions 9, 10a-10d, and 11a-11b) of "Satisfaction with OAB Control" module of OAB-s at each visit was summarized as a continuous variable.

King's Health Questionnaire: The total score of 9 domains of KHQ was summarized at enrollment and EOT visit using number of subjects, mean (and 95% CI for the mean), median, SD, minimum, and maximum.

Safety data collected in this study were summarized and listed according to the Sponsor's data standards.

RESULTS

Subject Disposition and Demography: A summary of subject disposition and analysis populations is provided in Table 2.

Table 2. Subject Disposition and Subjects Analyzed

Number of Subjects	Fesoterodine
Screened	31
Assigned to study treatment	31
Treated	31
Completed	20
Discontinued	11
Discontinuations	
Relation to study drug not defined	11
Insufficient clinical response	1
Lost to follow-up	4
No longer willing to participate in study	6
Analyzed for efficacy	
FAS	28
Analyzed for safety	
AEs	31

Discontinuations were attributed to the last study treatment received.
AE = adverse event; FAS = full analysis set

A summary of demographic characteristics is provided in Table 3. Ninety-seven percent of the study population were female. Fifteen subjects were <75 years old and 16 were ≥75 years old. The mean body mass index of study subjects was 28.2 kg/m^2.

Table 3. Demographic Characteristics

Parameter	Fesoterodine		
	Male	Female	Total
Number of Subjects	1	30	31
Age (years)			
<65	0	0	0
65-74	0	15	15
75-84	1	13	14
≥85	0	2	2
Mean	83.0	75.2	75.4
SD	0.0	5.9	6.0
Range	83-83	66-88	66-88
Race			
White	1	30	31
Weight (kg)			
Mean	70.0	68.4	68.4
SD	0.0	6.9	6.8
Range	70.0-70.0	55.0-82.4	55.0-82.4
N	1	30	31
BMI (kg/m^2)			
Mean	25.7	28.2	28.2
SD	0.0	3.4	3.4
Range	25.7-25.7	22.6-36.1	22.6-36.1
N	1	29	30
Height (cm)			
Mean	165.0	155.6	155.9
SD	0.0	5.6	5.8
Range	165-165	144-165	144-165
N	1	29	30

BMI was defined as weight/(height × 0.01)^2.
BMI = body mass index; N = number of subjects; SD = standard deviation.

Efficacy Results:

Mean Number of Micturition-Related Urgency Episodes per 24 Hours at End-of-Treatment:

The mean number of micturition-related urgency episodes per 24 hours at EOT, the primary endpoint of this study, was decreased compared to baseline as shown in Table 4.

Table 4. Summary of Mean Number of Micturition-Related Urgency Episodes per 24 Hours at End-of-Treatment - LOCF - Full Analysis Set

Urgency Episodes per 24 Hours	Fesoterodine
Baseline[a]	
N	28
Mean (SD)	10.49 (5.28)
95% CI for mean	(8.44, 12.54)
Median	9.8
Minimum, Maximum	(4.33, 28.67)
EOT[b]	
N	28
Mean (SD)	5.48 (6.01)
95% CI for mean	(3.15, 7.80)
Median	4.5
Minimum, Maximum	(0.00, 29.67)

CI = confidence interval; EOT = end-of-treatment; LOCF = last observation carried forward; N = number of subjects; SD = standard deviation.
a. Previous fesoterodine study baseline visit.
b. The EOT visit was performed when the study ended (31 December 2011), or if the subject withdrew (whichever was earlier).

Mean Number of Micturition-Related Urgency Episodes per 24 Hours at Each Visit:

Table 5 presents the results for the mean number of micturition-related urgency episodes per 24 hours at each visit (FAS, last observation carried forward [LOCF]). The results showed a decrease at Month 3 (following enrollment into this study), compared to previous fesoterodine study baseline, which was sustained until EOT.

Table 5. Summary of Mean Number of Micturition-Related Urgency Episodes per 24 Hours at Each Visit – LOCF – Full Analysis Set

	Fesoterodine			
Urgency Episodes per 24 hours	N	Mean	95% CI	Median
Baseline[a]	28	10.49	8.44, 12.54	9.8
Month 3	25	5.28	2.25, 8.31	1.0
Month 6	28	6.37	3.75, 8.98	5.0
Month 9	28	4.98	2.49, 7.46	4.0
Month 12	28	5.15	2.59, 7.72	2.8
Month 15	27	5.09	2.53, 7.64	3.7
Month 18	24	5.22	2.61, 7.83	4.0
EOT	28	5.48	3.15, 7.80	4.5

CI = confidence interval; EOT = end-of-treatment; LOCF = last observation carried forward; N = number of subjects.
a. Previous fesoterodine study baseline visit.

Results based on observed visits also demonstrated this sustained decrease in micturition-related urgency episodes per 24 hours (Table 6). A slight increase was noted at Month 6 in both the LOCF and observed visits analyses.

Table 6. Summary of Mean Number of Micturition-Related Urgency Episodes per 24 Hours at Each Visit - Observed Visits - Full Analysis Set

	Fesoterodine			
Urgency Episodes per 24 Hours	**N**	**Mean**	**95% CI**	**Median**
Baseline[a]	28	10.49	8.44, 12.54	9.8
Month 3	25	5.28	2.25, 8.31	1.0
Month 6	23	7.10	4.06, 10.14	5.7
Month 9	23	4.59	1.67, 7.52	1.7
Month 12	19	4.42	0.93, 7.91	1.7
Month 15	18	5.41	1.78, 9.03	3.0
Month 18	17	5.18	1.58, 8.77	3.0

CI = confidence interval; N = number of subjects.
a. Previous fesoterodine study baseline visit.

Mean Number of Severe Micturition-Related Urgency Episodes per 24 Hours at Each Visit:

Table 7 presents the results for the mean number of severe micturition-related urgency episodes per 24 hours at each visit (FAS, LOCF). The results showed a decrease at Month 3 (following enrollment into this study), compared to previous fesoterodine study baseline, which was sustained until EOT.

Table 7. Summary of Mean Number of Severe Micturition-Related Urgency Episodes per 24 Hours at Each Visit - LOCF - Full Analysis Set

	Fesoterodine			
Severe Urgency Episodes per 24 Hours	**N**	**Mean**	**95% CI**	**Median**
Baseline[a]	28	6.35	3.67, 9.02	4.0
Month 3	25	3.36	0.41, 6.31	0.0
Month 6	28	2.40	0.02, 4.79	0.0
Month 9	28	2.52	0.26, 4.79	0.2
Month 12	28	2.23	-0.05, 4.50	0.0
Month 15	27	2.67	-0.26, 5.07	0.0
Month 18	24	2.44	-0.20, 5.09	0.0
EOT	28	2.29	0.03, 4.55	0.0

CI = confidence interval; EOT = end-of-treatment; LOCF = last observation carried forward; N = number of subjects.
a. Previous fesoterodine study baseline visit.

Results based on observed visits also demonstrated this sustained decrease in severe micturition-related urgency episodes per 24 hours (Table 8).

Table 8. Summary of Mean Number of Severe Micturition-Related Urgency Episodes per 24 Hours at Each Visit - Observed Visits - Full Analysis Set

	Fesoterodine			
Severe Urgency Episodes per 24 Hours	**N**	**Mean**	**95% CI**	**Median**
Baseline[a]	28	6.35	3.67, 9.02	4.0
Month 3	25	3.36	0.41, 6.31	0.0
Month 6	23	2.72	-0.18, 5.63	0.0
Month 9	23	2.72	-0.04, 5.49	0.0
Month 12	19	2.37	-0.96, 5.70	0.0
Month 15	18	3.30	-0.36, 6.95	0.0
Month 18	17	2.39	-1.35, 6.13	0.0

CI = confidence interval; N = number of subjects.
a. Previous fesoterodine study baseline visit.

Mean Number of Micturitions per 24 Hours at Each Visit:

Table 9 presents the results for the mean number of micturitions per 24 hours at each visit (FAS, LOCF). The results showed a decrease at Month 3 (following enrollment into this study), compared to previous fesoterodine study baseline, which was sustained until EOT.

Table 9. Summary of Mean Number of Micturitions per 24 Hours at Each Visit - LOCF - Full Analysis Set

	Fesoterodine			
Micturitions per 24 Hours	**N**	**Mean**	**95% CI**	**Median**
Baseline[a]	28	13.44	11.67, 15.21	11.3
Month 3	25	10.97	9.03, 12.92	10.0
Month 6	28	10.98	9.33, 12.63	10.2
Month 9	28	10.44	8.79, 12.09	9.5
Month 12	28	10.51	8.78, 12.24	10.2
Month 15	27	10.67	9.07, 12.28	10.0
Month 18	24	10.60	8.73, 12.46	10.0
EOT	28	10.38	8.75, 12.01	9.8

CI = confidence interval; EOT = end-of-treatment; LOCF = last observation carried forward; N = number of subjects.
a. Previous fesoterodine study baseline visit.

Results based on observed visits also demonstrated this sustained decrease in micturitions per 24 hours (Table 10).

Table 10. Summary of Mean Number of Micturitions per 24 Hours at Each Visit - Observed Visits - Full Analysis Set

	Fesoterodine			
Micturitions per 24 Hours	**N**	**Mean**	**95% CI**	**Median**
Baseline[a]	28	13.44	11.67, 15.21	11.3
Month 3	25	10.97	9.03, 12.92	10.0
Month 6	23	11.22	9.20, 13.24	10.3
Month 9	23	10.58	8.59, 12.57	9.3
Month 12	19	10.61	8.10, 13.12	10.3
Month 15	18	10.53	8.08, 12.98	9.3
Month 18	17	10.73	8.03, 13.42	9.7

CI = confidence interval; N = number of subjects.
a. Previous fesoterodine study baseline visit.

Number of Night-Time Micturitions per 24 Hours at Each Visit:

Table 11 presents the results for the mean number of night-time micturitions per 24 hours at each visit (FAS, LOCF). The results showed a small mean decrease at Month 3 (following enrollment into this study), but the median shows a slight increase, compared to previous fesoterodine study baseline. However a consistent decrease compared to baseline was sustained from Month 6 until EOT.

Table 11. Summary of Mean Number of Night-Time Micturitions per 24 Hours at Each Visit - LOCF - Full Analysis Set

	Fesoterodine			
Night-Time Micturitions per 24 Hours	**N**	**Mean**	**95% CI**	**Median**
Baseline[a]	28	3.45	2.86, 4.05	3.2
Month 3	25	3.08	2.29, 3.87	3.3
Month 6	28	3.25	2.58, 3.92	3.0
Month 9	28	3.07	2.33, 3.81	3.0
Month 12	28	2.88	2.11, 3.65	2.8
Month 15	27	3.00	2.21, 3.79	2.7
Month 18	24	2.95	2.08, 3.82	2.8
EOT	28	2.95	2.15, 3.74	2.6

CI = confidence interval; EOT = end-of-treatment; LOCF = last observation carried forward; N = number of subjects.
a. Previous fesoterodine study baseline visit.

Results based on observed visits also demonstrated this sustained decrease in night-time micturitions per 24 hours (Table 12).

Table 12. Summary of Mean Number of Night-Time Micturitions per 24 Hours at Each Visit - Observed Visits - Full Analysis Set

	Fesoterodine			
Night-Time Micturitions per 24 Hours	**N**	**Mean**	**95% CI**	**Median**
Baseline[a]	28	3.45	2.86, 4.05	3.2
Month 3	25	3.08	2.29, 3.87	3.3
Month 6	23	3.22	2.43, 4.00	3.0
Month 9	23	2.99	2.15, 3.82	3.0
Month 12	19	2.82	1.78, 3.86	2.7
Month 15	18	2.57	1.49, 3.65	2.2
Month 18	17	2.81	1.61, 4.02	2.5

CI = confidence interval; N = number of subjects.
a. Previous fesoterodine study baseline visit.

Mean Number of Urgency Urinary Incontinence Episodes per 24 hours at Each Visit:

Table 13 presents the results for the mean number of UUI episodes per 24 hours at each visit (FAS, LOCF). The results showed a small decrease at Month 3 (following enrollment into this study), compared to previous fesoterodine study baseline. Results were generally sustained until EOT, with a small increase at Month 15.

One outlier, one subject, reported almost 30 UUI episodes per 24 hours at each visit. However, for both the LOCF and observed visits analyses, the medians at each visit with the exception of baseline were 0.

Table 13. Summary of Mean Number of Urgency Urinary Incontinence Episodes per 24 Hours at Each Visit - LOCF - Full Analysis Set

	Fesoterodine			
UUI Episodes per 24 Hours	**N**	**Mean**	**95% CI**	**Median**
Baseline[a]	28	2.64	0.59, 4.70	0.8
Month 3	25	2.27	-0.57, 5.10	0.0
Month 6	28	1.54	-0.70, 3.77	0.0
Month 9	28	1.36	-0.82, 3.54	0.0
Month 12	28	1.29	-0.92, 3.49	0.0
Month 15	27	1.83	-0.54, 4.20	0.0
Month 18	24	1.65	-0.91, 4.21	0.0
EOT	28	1.49	-0.69, 3.67	0.0

CI = confidence interval; EOT = end-of-treatment; LOCF = last observation carried forward; N = number of subjects; UUI = urgency urinary incontinence.
a. Previous fesoterodine study baseline visit.

Results based on observed visits demonstrated a similar pattern (Table 14).

Table 14. Summary of Mean Number of Urgency Urinary Incontinence Episodes per 24 Hours at Each Visit - Observed Visits - Full Analysis Set

	Fesoterodine			
UUI Episodes per 24 Hours	**N**	**Mean**	**95% CI**	**Median**
Baseline[a]	28	2.64	0.59, 4.70	0.8
Month 3	25	2.27	-0.57, 5.10	0.0
Month 6	23	1.87	-0.87, 4.61	0.0
Month 9	23	1.65	-1.02, 4.33	0.0
Month 12	19	1.67	-1.64, 4.98	0.0
Month 15	18	2.69	-0.92, 6.29	0.0
Month 18	17	2.08	-1.61, 5.77	0.0

CI = confidence interval; EOT = end-of-treatment; LOCF = last observation carried forward; N = number of subjects; UUI = urgency urinary incontinence.
a. Previous fesoterodine study baseline visit.

Daily Sum Rating in the Urinary Sensation Scale:

Table 15 presents the results for the daily sum rating in the USS at each visit (FAS, LOCF). The results showed a decrease at Month 3 (following enrollment into this study), compared to previous fesoterodine study baseline, which was sustained until EOT.

Table 15. Summary of Daily Sum Rating in the Urinary Sensation Scale at Each Visit - LOCF - Full Analysis Set

	Fesoterodine			
USS Daily Sum Rating	**N**	**Mean**	**95% CI**	**Median**
Baseline[a]	28	45.63	36.43, 54.83	39.2
Month 3	25	31.60	19.08, 44.12	23.3
Month 6	28	31.39	21.27, 41.51	25.2
Month 9	28	28.29	18.30, 38.27	23.3
Month 12	28	27.63	17.29, 37.97	22.2
Month 15	27	28.67	18.26, 39.07	22.3
Month 18	24	29.01	17.67, 40.36	23.2
EOT	28	28.60	18.84, 38.35	23.2

CI = confidence interval; EOT = end-of-treatment; LOCF = last observation carried forward; N = number of subjects; USS = urgency sensation scale.
a. Previous fesoterodine study baseline visit.

Results based on observed visits also demonstrated this sustained decrease in the daily sum rating in the USS (Table 16).

Table 16. Summary of Daily Sum Rating in the Urinary Sensation Scale at Each Visit - Observed Visits - Full Analysis Set

	Fesoterodine			
USS Daily Sum Rating	**N**	**Mean**	**95% CI**	**Median**
Baseline[a]	28	45.63	36.43, 54.83	39.2
Month 3	25	31.60	19.08, 44.12	23.3
Month 6	23	33.25	20.96, 45.53	25.7
Month 9	23	28.38	16.15, 40.60	23.3
Month 12	19	26.98	11.90, 42.06	19.0
Month 15	18	30.20	14.43, 45.98	21.5
Month 18	17	29.53	13.27, 45.78	22.0

CI = confidence interval; EOT = end-of-treatment; LOCF = last observation carried forward; N = number of subjects; USS = urgency sensation scale.
a. Previous fesoterodine study baseline visit.

Number and Percentage of Subjects Who Were Incontinent at Enrollment Visit and Were Dry in the 3 Days Prior to Each Visit:

Table 17 presents the results for the frequency and percentage of dry subjects with UUI >0 at enrollment by visit (FAS, LOCF). The results showed that the number of subjects dry was relatively consistent from Month 3 (following enrollment into this study) to EOT.

Table 17. Frequency Count and Percentage of Dry Subjects at Each Visit - LOCF - Full Analysis Set (For Subjects With Urgency Urinary Incontinence Greater Than 0 at Enrollment)

	Fesoterodine		
	N	n	(%)
Subjects incontinent at Baseline[a]	31	18	(58.1)
Subjects dry at[b]:			
Month 3	16	13	(81.3)
Month 6	18	14	(77.8)
Month 9	18	14	(77.8)
Month 12	18	14	(77.8)
Month 15	17	11	(64.7)
Month 18	15	10	(66.7)
EOT	18	12	(66.7)

CI = confidence interval; EOT = end-of-treatment; LOCF = last observation carried forward.
a. Previous fesoterodine study baseline visit.
b. N = number of subjects incontinent in previous fesoterodine study baseline with diary data in this study; n = number of dry subjects.

Results were similar for observed visits, though there was a slight decrease in the number of subjects dry at later visits (Table 18).

Table 18. Frequency Count and Percentage of Dry Subjects at Each Visit - Observed Visits - Full Analysis Set (For Subjects With Urgency Urinary Incontinence Greater Than 0 at Enrollment)

	Fesoterodine		
	N	n	(%)
Subjects incontinent at Baseline[a]	31	18	(58.1)
Subjects dry at[b]:			
Month 3	16	13	(81.3)
Month 6	16	12	(75.0)
Month 9	16	12	(75.0)
Month 12	13	10	(76.9)
Month 15	15	10	(66.7)
Month 18	12	9	(75.0)

CI = confidence interval.
a. Previous fesoterodine study baseline visit.
b. N = number of subjects incontinent in previous fesoterodine study baseline with diary data in this study; n = number of dry subjects.

Number of Urinary Incontinence Pads, Barrier Creams, and Powder (For Skin Protection):

Table 19 presents the results for the mean number of urinary incontinence pads, barrier creams, and powder (for skin protection) for subjects with UUI >0 at enrollment by visit (FAS, LOCF). Results for the mean number of urinary incontinence pads, barrier creams, and powder for subjects with UUI >0 at enrollment were variable, but median results showed decreases over time for incontinence pads and a median of 0 barrier creams and powders per 24 hours for all visits.

Table 19. Summary of Mean Number of Urinary Incontinence Pads, Barrier Creams, and Powder (For Skin Protection) per 24 Hours At Each Visit - LOCF - Full Analysis Set (Subjects With Urgency Urinary Incontinence Greater Than 0 at Enrollment)

	Fesoterodine			
	N	Mean	95% CI	Median
Incontinence pads per 24 hours				
Baseline[a]	18	3.69	2.34, 5.03	3.3
Month 3	16	3.15	0.68, 5.61	2.0
Month 6	18	3.02	0.90, 5.14	2.2
Month 9	18	2.56	1.39, 3.72	2.0
Month 12	18	2.52	1.31, 3.73	2.0
Month 15	17	2.45	1.26, 3.64	2.0
Month 18	15	2.49	1.26, 3.72	2.0
EOT	18	2.31	1.27, 3.36	2.0
Creams per 24 hours				
Baseline[a]	18	0.48	0.03, 0.93	0.0
Month 3	16	0.79	-0.31, 1.89	0.0
Month 6	18	0.43	-0.08, 0.93	0.0
Month 9	18	0.33	-0.20, 0.87	0.0
Month 12	18	0.13	-0.14, 0.40	0.0
Month 15	17	0.18	-0.10, 0.45	0.0
Month 18	15	0.18	-0.12, 0.47	0.0
EOT	18	0.15	-0.09, 0.39	0.0
Powder per 24 hours				
Baseline[a]	18	0.24	-0.27, 0.75	0.0
Month 3	16	0.19	-0.21, 0.59	0.0
Month 6	18	0.20	-0.23, 0.63	0.0
Month 9	18	0.17	-0.18, 0.52	0.0
Month 12	18	0.31	-0.35, 0.98	0.0
Month 15	17	0.00	0.00, 0.00	0.0
Month 18	15	0.00	0.00, 0.00	0.0
EOT	18	0.00	0.00, 0.00	0.0

CI = confidence interval; EOT = end-of-treatment; LOCF = last observation carried forward; N = number of subjects.
a. Previous fesoterodine study baseline visit.

Similar results were observed based on observed visits (Table 20).

Table 20. Summary of Mean Number of Urinary Incontinence Pads, Barrier Creams and Powder (For Skin Protection) per 24 Hours At Each Visit - Observed Visits - Full Analysis Set (Subjects With Urgency Urinary Incontinence Greater Than 0 at Enrollment)

	Fesoterodine			
	N	Mean	95% CI	Median
Incontinence pads per 24 Hours				
Baseline[a]	18	3.69	2.34, 5.03	3.3
Month 3	16	3.15	0.68, 5.61	2.0
Month 6	16	3.15	0.77, 5.52	2.2
Month 9	16	2.56	1.27, 3.86	2.0
Month 12	13	2.44	1.12, 3.75	2.0
Month 15	15	2.27	0.93, 3.61	1.7
Month 18	12	1.94	0.63, 3.26	2.0
Creams per 24 hours				
Baseline[a]	18	0.48	0.03, 0.93	0.0
Month 3	16	0.79	-0.31, 1.89	0.0
Month 6	16	0.48	-0.09, 1.04	0.0
Month 9	16	0.38	-0.23, 0.98	0.0
Month 12	13	0.18	-0.21, 0.57	0.0
Month 15	15	0.20	-0.11, 0.51	0.0
Month 18	12	0.22	-0.15, 0.60	0.0
Powder per 24 hours				
Baseline[a]	18	0.24	-0.27, 0.75	0.0
Month 3	16	0.19	-0.21, 0.59	0.0
Month 6	16	0.23	-0.26, 0.72	0.0
Month 9	16	0.19	-0.21, 0.59	0.0
Month 12	13	0.44	-0.51, 1.39	0.0
Month 15	15	0.00	0.00, 0.00	0.0
Month 18	12	0.00	0.00, 0.00	0.0

CI = confidence interval; N = number of subjects.
a. Previous fesoterodine study baseline visit.

Evaluations Based on Subject's Questionnaires:

Patient Perception of Bladder Condition:

A frequency table of change from enrollment visit in PPBC results (LOCF, FAS) is presented in Table 21. The majority of subjects reported either an 'Improvement" (score difference <0) or "No Change" (score difference = 0) in bladder condition at each visit; approximately 20% of subjects at each visit experienced "Deterioration" (score difference ≥1) in bladder condition.

Table 21. Frequency Table of Change From Enrollment Visit Response of Patient Perception of Bladder Condition at Each Visit – LOCF - Full Analysis Set

		Fesoterodine (N=28)	
		n	(%)
Month 3	N	27	
	Deterioration (score difference ≥1)	6	(22.2)
	No change (score difference = 0)	9	(33.3)
	Improvement (score difference <0)	12	(44.4)
Month 6	N	28	
	Deterioration (score difference ≥1)	6	(21.4)
	No change (score difference = 0)	12	(42.9)
	Improvement (score difference <0)	10	(35.7)
Month 9	N	28	
	Deterioration (score difference ≥1)	6	(21.4)
	No change (score difference = 0)	12	(42.9)
	Improvement (score difference <0)	10	(35.7)
Month 12	N	28	
	Deterioration (score difference ≥1)	5	(17.9)
	No change (score difference = 0)	12	(42.9)
	Improvement (score difference <0)	11	(39.3)
Month 15	N	27	
	Deterioration (score difference ≥1)	6	(22.2)
	No change (score difference = 0)	10	(37.0)
	Improvement (score difference <0)	11	(40.7)
Month 18	N	24	
	Deterioration (score difference ≥1)	6	(25.0)
	No change (score difference = 0)	6	(25.0)
	Improvement (score difference <0)	12	(50.0)
EOT	N	28	
	Deterioration (score difference ≥1)	6	(21.4)
	No change (score difference = 0)	9	(32.1)
	Improvement (score difference <0)	13	(46.4)

Analyses at each time point are based on visit windows as specified in the SAP.
EOT = end-of-treatment; LOCF = last observation carried forward; N = number of subjects; n = number of subjects with specified criteria; SAP = statistical analysis plan.

Patient Perception of Urgency Scale:

A frequency table of change from enrollment visit in PPUS results (LOCF, FAS) is presented in Table 22. The majority of subjects reported "No Change" (difference of scores was 0) at all visits.

Table 22. Frequency Table of Change From Enrollment Visit Response of Patient Perception of Urgency Scale at Each Visit - LOCF - Full Analysis Set

		Fesoterodine (N=28)	
		n	(%)
Month 3	N	27	
	Deterioration = negative difference of scores	5	(18.5)
	No change = difference of scores is 0	17	(63.0)
	Improvement = increase of 1 or more points in difference of scores	5	(18.5)
Month 6	N	28	
	Deterioration = negative difference of scores	9	(32.1)
	No change = difference of scores is 0	13	(46.4)
	Improvement = increase of 1 or more points in difference of scores	6	(21.4)
Month 9	N	28	
	Deterioration = negative difference of scores	7	(25.0)
	No change = difference of scores is 0	19	(67.9)
	Improvement = increase of 1 or more points in difference of scores	2	(7.1)
Month 12	N	28	
	Deterioration = negative difference of scores	7	(25.0)
	No change = difference of scores is 0	17	(60.7)
	Improvement = increase of 1 or more points in difference of scores	4	(14.3)
Month 15	N	27	
	Deterioration = negative difference of scores	5	(18.5)
	No change = difference of scores is 0	19	(70.4)
	Improvement = increase of 1 or more points in difference of scores	3	(11.1)
Month 18	N	24	
	Deterioration = negative difference of scores	6	(25.0)
	No change = difference of scores is 0	12	(50.0)
	Improvement = increase of 1 or more points in difference of scores	6	(25.0)
EOT	N	28	
	Deterioration = negative difference of scores	6	(21.4)
	No change = difference of scores is 0	16	(57.1)
	Improvement = increase of 1 or more points in difference of scores	6	(21.4)

Analyses at each time point are based on visit windows as specified in the SAP.
EOT = end-of-treatment; LOCF = last observation carried forward; N = number of subjects; n = number of subjects with specified criteria; SAP = statistical analysis plan.

Overactive Bladder Questionnaire (33 Questions):

A summary of OAB-q for the total health related quality of life (HRQL) score at each visit (LOCF, FAS) is presented in Table 23. Mean total HRQL scores were similar over the entire treatment period.

Table 23. Summary of OAB-q - Total HRQL Score at Each Visit - LOCF - Full Analysis Set

	Fesoterodine			
	N	Mean	95% CI	Median
Enrollment	28	77.09	70.85, 83.33	79.2
Month 3	27	77.87	70.05, 85.69	79.2
Month 6	28	76.65	70.12, 83.18	79.2
Month 9	28	79.14	72.03, 86.25	80.0
Month 12	28	76.42	69.35, 83.49	77.6
Month 15	27	75.01	66.56, 83.47	78.4
Month 18	24	78.02	70.09, 85.96	77.6
EOT	28	77.59	70.49, 84.70	77.6

Analyses at each time point are based on visit windows as specified in the SAP.
CI = confidence interval; EOT = end-of-treatment; HRQL = health-related quality of life; LOCF = last observation carried forward; N = number of subjects; OAB-q = Overactive Bladder Questionnaire; SAP = statistical analysis plan.

A summary of OAB-q for the subscale scores of HRQL at enrollment and EOT visits (LOCF, FAS) is presented in Table 24. Mean scores were slightly higher (ie, worsened) at EOT, as compared to enrollment, for the coping, concern, and sleep subscales. The mean score for the social subscale was slightly lower (ie, improved) at EOT, as compared to enrollment.

Table 24. Summary of OAB-q Subscale Scores of HRQL at Enrollment and End-of-Treatment Visit - LOCF - Full Analysis Set

		Fesoterodine			
OAB-q Domain	Visit	N	Mean	95% CI	Median
Coping subscale score	Enrollment	28	77.77	70.13, 85.40	80.0
	EOT	28	79.29	72.25, 86.32	80.0
Concern subscale score	Enrollment	28	71.04	64.02, 78.05	68.6
	EOT	28	72.35	64.09, 80.60	68.6
Sleep subscale score	Enrollment	28	71.00	63.35, 78.65	76.0
	EOT	28	73.57	65.38, 81.76	80.0
Social subscale score	Enrollment	28	90.57	86.52, 94.63	92.0
	EOT	28	86.25	79.78, 92.72	84.0

Analyses at each time point are based on visit windows as specified in the SAP.
CI = confidence interval; EOT = end-of-treatment; HRQL = health-related quality of life; LOCF = last observation carried forward; N = number of subjects; OAB-q = Overactive Bladder Questionnaire; SAP = statistical analysis plan.

Similar results were obtained for the observed visits analysis (Table 25).

Table 25. Summary of OAB-q Subscale Scores of HRQL at Enrollment and End-of-Treatment Visit - Observed Visits - Full Analysis Set

		Fesoterodine			
OAB-q Domain	**Visit**	**N**	**Mean**	**95% CI**	**Median**
Coping Subscale Score	Enrollment	28	77.77	70.13, 85.40	80.0
	Month 18	20	79.50	70.42, 88.58	80.0
Concern Subscale Score	Enrollment	28	71.04	64.02, 78.05	68.6
	Month 18	20	71.29	61.12, 81.46	68.6
Sleep Subscale Score	Enrollment	28	71.00	63.35, 78.65	76.0
	Month 18	20	72.00	61.36, 82.64	80.0
Social Subscale Score	Enrollment	28	90.57	86.52, 94.63	92.0
	Month 18	20	86.20	77.56, 94.84	84.0

Analyses at each time point are based on visit windows as specified in the SAP.
CI = confidence interval; HRQL = health-related quality of life; N = number of subjects; OAB-q = Overactive Bladder Questionnaire; SAP = statistical analysis plan.

Overactive Bladder Satisfaction Questionnaire:

A summary of the OAB-s proportion of responders to Question 5 (Medication Expectation) at each visit (LOCF, FAS) is presented in Table 26. The majority of subjects reported "exceeding/meeting expectations" at all visits.

Table 26. Frequency Table for OAB-s - Proportion of Responders to Question 5 (Medication Expectation) at Each Visit - LOCF - Full Analysis Set

		Fesoterodine (N=28)	
		n	**(%)**
Enrollment	N	26	
	Exceeding/meeting expectations	22	(84.6)
	Does not meet expectations	4	(15.4)
Month 3	N	27	
	Exceeding/meeting expectations	22	(81.5)
	Does not meet expectations	5	(18.5)
Month 6	N	28	
	Exceeding/meeting expectations	25	(89.3)
	Does not meet expectations	3	(10.7)
Month 9	N	28	
	Exceeding/meeting expectations	25	(89.3)
	Does not meet expectations	3	(10.7)
Month 12	N	28	
	Exceeding/meeting expectations	24	(85.7)
	Does not meet expectations	4	(14.3)
Month 15	N	27	
	Exceeding/meeting expectations	23	(85.2)
	Does not meet expectations	4	(14.8)
Month 18	N	24	
	Exceeding/meeting expectations	19	(79.2)
	Does not meet expectations	5	(20.8)
EOT	N	28	
	Exceeding/meeting expectations	23	(82.1)
	Does not meet expectations	5	(17.9)

Analyses at each time point were based on visit windows as specified in the SAP.
A responder was defined as a subject who answered, "Greatly exceeds my expectations," "Somewhat exceeds my expectations," or "Meets my expectations" to Question 5.
EOT = end-of-treatment; LOCF = last observation carried forward; N = number of subjects; n = number of subjects with specified criteria; OAB-s = Overactive Bladder Satisfaction Questionnaire; SAP = statistical analysis plan.

A summary of the OAB-s proportion of responders Questions 9, 10a-10d, and 11a-11b (satisfaction with medication) at each visit (LOCF, FAS) is presented in Table 27. The majority of subjects reported "satisfied" at all visits.

Table 27. Frequency Table for OAB-s - Proportion of Responders to Questions 9, 10a-10d, and 11a-11b (Satisfaction With Medication) at Each Visit - LOCF - Full Analysis Set

		Fesoterodine (N=28)	
		n	(%)
Enrollment	N	27	
	Satisfied	19	(70.4)
	Not satisfied	8	(29.6)
Month 3	N	26	
	Satisfied	17	(65.4)
	Not satisfied	9	(34.6)
Month 6	N	27	
	Satisfied	15	(55.6)
	Not satisfied	12	(44.4)
Month 9	N	27	
	Satisfied	16	(59.3)
	Not satisfied	11	(40.7)
Month 12	N	27	
	Satisfied	16	(59.3)
	Not satisfied	11	(40.7)
Month 15	N	26	
	Satisfied	17	(65.4)
	Not satisfied	9	(34.6)
Month 18	N	24	
	Satisfied	16	(66.7)
	Not satisfied	8	(33.3)
EOT	N	27	
	Satisfied	18	(66.7)
	Not satisfied	9	(33.3)

Analyses at each time point were based on visit windows as specified in the SAP.
A responder was defined as a subject who answered "Very satisfied" or "Somewhat satisfied" on all of the 7 items.
EOT = end-of-treatment; LOCF = last observation carried forward; N = number of subjects; n = number of subjects with specified criteria; OAB-s = Overactive Bladder Satisfaction Questionnaire; SAP = statistical analysis plan.

King's Health Questionnaire:

Results for the KHQ were variable, with some domain scores higher at EOT and some domain scores lower at EOT. A summary of total domain scores of KHQ at the enrollment and EOT visits is provided for observed visits in Table 28.

Table 28. Summary of Total Domain Scores of King's Health Questionnaire at Enrollment and End-of-Treatment Visit - Observed Visits - Full Analysis Set

		Fesoterodine			
KHQ Domain	**Visit**	**N**	**Mean**	**95% CI**	**Median**
General health perception score	Enrollment	28	43.75	35.56, 51.94	50.0
	EOT	20	38.75	27.70, 49.80	25.0
Incontinence impact score	Enrollment	27	50.62	41.39, 59.85	33.3
	EOT	20	41.67	29.40, 53.93	33.3
Role limitations score	Enrollment	27	31.48	20.77, 42.20	33.3
	EOT	20	35.00	20.93, 49.07	33.3
Physical limitations score	Enrollment	27	37.04	25.00, 49.07	33.3
	EOT	20	34.17	22.17, 46.16	33.3
Social limitations score	Enrollment	27	13.99	4.42, 23.56	0.0
	EOT	20	20.56	9.08, 32.03	16.7
Personal relationships score	Enrollment	11	1.52	-1.86, 4.89	0.0
	EOT	10	11.67	-2.16, 25.49	0.0
Emotions score	Enrollment	27	35.80	25.65, 45.95	33.3
	EOT	20	32.78	22.18, 43.38	33.3
Sleep/energy score	Enrollment	27	34.57	25.44, 43.70	33.3
	EOT	20	35.00	24.29, 45.71	33.3
Severity of urinary symptoms score	Enrollment	27	44.69	36.04, 53.34	46.7
	EOT	20	42.33	32.30, 52.37	46.7

KHQ domain scores: 0 = best; 100 = worst. A higher score indicates worse QOL.
CI = confidence interval; EOT = end-of-treatment; KHQ = King's Health Questionnaire; N = number of subjects; QOL = quality of life.

Safety Results:

Treatment-Emergent Adverse Events (TEAEs; All-Causality): Table 29 presents the TEAEs (all-causality) by system organ class (SOC) and preferred term.

Table 29. Incidence of Treatment-Emergent Adverse Events (All-Causality)

Number of Subjects With Adverse Events by: System Organ Class MedDRA (v14.1) Preferred Term	Fesoterodine (N=31) n (%)
Number of subjects with adverse events	9 (29.0)
Gastrointestinal disorders	3 (9.7)
Dry mouth	2 (6.5)
Nausea	1 (3.2)
General disorders and administration site conditions	2 (6.5)
Gait disturbance	1 (3.2)
Malaise	1 (3.2)
Oedema peripheral	1 (3.2)
Infections and infestations	3 (9.7)
Urinary tract infection	3 (9.7)
Investigations	1 (3.2)
Blood glucose decreased	1 (3.2)
Psychiatric disorders	1 (3.2)
Depression	1 (3.2)
Reproductive system and breast disorders	1 (3.2)
Vulvovaginal discomfort	1 (3.2)
Respiratory, thoracic and mediastinal disorders	1 (3.2)
Cough	1 (3.2)
Skin and subcutaneous tissue disorders	1 (3.2)
Cold sweat	1 (3.2)

Subjects were counted only once per treatment in each row.
Included data up to 7 days after last dose of study drug.
MedDRA (version 14.1) coding dictionary applied.
AE = adverse event; MedDRA (v14.1) = Medical Dictionary for Regulatory Activities (version 14.1); N = total number of subjects; n = number of subjects with adverse events.

Treatment-Related Treatment-Emergent Adverse Events: Table 30 presents treatment-related TEAEs reported during the study.

Table 30. Incidence of Treatment-Related Treatment-Emergent Adverse Events

System Organ Class MedDRA (v14.1) Preferred Term	Fesoterodine (N=31) n
Total preferred term events	4
Gastrointestinal disorders	2
Dry mouth	2
General disorders and administration site conditions	1
Gait disturbance	1
Oedema peripheral	1

Subjects were counted only once per treatment in each row.
Included data up to 7 days after last dose of study drug.
MedDRA (version 14.1) coding dictionary applied.
AE = adverse event; MedDRA (v14.1) = Medical Dictionary for Regulatory Activities (version 14.1); N = number of evaluable subjects; n = number of treatment-related adverse events.

Serious Adverse Events (SAEs): One subject experienced a SAE during the study. The SAE, an event of "epilepsy" in a 69-year-old white female with a known history of epilepsy, was not considered to be treatment-related and resolved by the end of the study.

No treatment related SAEs were reported during the study.

Permanent Discontinuations due to Adverse Events: No subjects permanently discontinued due to AEs during this study.

Deaths: No deaths were reported during the study.

Concomitant Drug and Nondrug Treatments: All 31 subjects used at least 1 drug treatment concomitant with the study drug. The most common concomitant drug treatments were trimetazidine, acetylsalicylic acid, digoxin, gliclazide, omeprazole, paracetamol, and simvastatin. No concomitant nondrug treatments were reported during this study.

Drug Compliance: Subjects with a treatment compliance <80% or >120% for ≥2 visits, were identified as protocol deviators. They included 8 subjects with "<80% compliance with study treatment (or % compliance missing)".

Vital signs and Physical Examination: The mean changes from enrollment in vital signs (overall and by presence of hypertension) were not clinically meaningful. There were no reported physical examination abnormalities.

CONCLUSIONS:

- The results from both the primary endpoint and the key secondary endpoint micturition frequency suggest that the decrease in symptoms from the previous 24-week (12 weeks double-blind and 12 weeks open-label) randomized, placebo-controlled fesoterodine study baseline to the 3 months time point in this study was sustained until EOT. This likely represents a clinically meaningful maintenance of effect. Results for the subject-reported outcomes (PPBC and OAB-q) were maintained at a consistent level from enrollment and throughout the study, again suggesting maintenance of efficacy.

- Overall, fesoterodine was well-tolerated in the open label extension study and the tolerability and safety data in this elderly population are consistent with those observed in prior fesoterodine studies.