CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
21287s016

STATISTICAL REVIEW(S)

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Translational Sciences
Office of Biostatistics

STATISTICAL REVIEW AND EVALUATION

CLINICAL STUDIES

NDA/Serial Number:	21-287/N0015
Drug Name:	Uroxatral (Alfuzosin HCL)
Indication(s):	Treatment of pediatric patients aged 2 to 16 years with elevated leak point pressure associated with a known neurological disorder
Applicant:	Sanofi Aventis US LLC
Date(s):	Date of submission: 06/16/2010
	PDUFA due date: 12/16/2010
	Review completion date: 11/16/2010
Review Priority:	Priority
Biometrics Division:	Division of Biometrics 3
Statistical Reviewer:	Xin Fang, Ph.D.
Concurring Reviewer:	Sonia Castillo, Ph.D., Acting Team Leader
Medical Division:	Division of Reproductive and Urologic Products
Clinical Team:	Christine P, Nguyen, MD, Clinical Reviewer
	Suresh Kaul, MD, Clinical Team Leader
Project Manager:	George Lyght

Keywords: NDA review, Pediatric Written Request, ANCOVA

Table of Contents

1. EXECUTIVE SUMMARY

1.1 Conclusions and Recommendations

From a statistical perspective, the data from a study conducted under a Pediatric Written Request do not support either the 0.1 mg/kg/day or 0.2 mg/kg/day alfuzosin dose for the treatment of pediatric patients aged 2 to 16 years with elevated leak point pressure (LPP) associated with a known neurological disorder based on the proportion of patients with detrusor LLP < 40 cm H_2O. Descriptively, the proportion of patients with detrusor LLP < 40 cm H_2O was 48.3% in the 0.2 mg/kg/day alfuzosin group, 40.4% in the 0.1 mg/kg/day alfuzosin group, and 40.4% in the placebo group.

1.2 Brief Overview of Clinical Studies

The sponsor, Sanofi-Aventis US LLC, completed the three studies listed in the Pediatric Written Request dated 02/21/2006 and submitted all related data in support of alfuzosin for the treatment of pediatric patients aged 2 to 16 years with elevated leak point pressure associated with a known neurological disorder. Alfuzosin was approved for the treatment of the signs and symptoms of benign prostatic hyperplasia in adults on 06/12/2003.

Two of the three studies were exploratory and the third study was pivotal. The focus of this review is Study EFC5722, a randomized, double-blind, placebo-controlled, multicenter (49 sites), multinational (15 countries), parallel-group trial conducted in 172 pediatric patients over 12 weeks. Patients were equally randomized to one of three treatment groups: placebo, 0.1 mg/kg/day alfuzosin, and 0.2 mg/kg/day alfuzosin.

The primary objective of Study EFC5722 was to evaluate the efficacy of two alfuzosin doses compared to placebo based on detrusor leak point pressure (LPP) of neuropathic etiology in pediatric patients aged 2-16 with an elevated detrusor LPP and detrusor LPP ≥ 40 cm H_2O. The primary efficacy variable was the proportion of patients with detrusor LPP < 40 cm H_2O.

1.3 Statistical Issues and Findings

There were no statistical issues in the efficacy evaluation. There was an unexpectedly high placebo response rate seen in this study. The proportion of pediatric patients with detrusor LPP < 40 cm H_2O in the placebo group at Week 12 was 40.4%, greater than the assumed proportion of 10% used for sample size calculation. For comparison, the proportions in both alfuzosin doses are close to the assumed proportion of 50%.

Neither the 0.1 mg/kg/day nor the 0.2 mg/kg/day alfuzosin dose demonstrated efficacy for the treatment of pediatric patients aged 2 to 16 years with elevated leak point pressure (LPP) associated with a known neurological disorder based on the proportion of patients with detrusor LLP < 40 cm H_2O. Descriptively, the proportion of patients with detrusor LLP < 40 cm H_2O was 48.3% in the 0.2 mg/kg/day alfuzosin group, 40.4% in the 0.1 mg/kg/day alfuzosin group, and 40.4% in the placebo group.

2. INTRODUCTION

2.1 Overview

The applicant, Sanofi-Aventis US LLC, submitted information from three studies conducted under a Pediatric Written Request in support of alfuzosin for the treatment of pediatric patients aged 2 to 16 years with elevated leak point pressure associated with a known neurological disorder. Two of the three pediatric studies were open-label and exploratory and one, Study EFC5722, was pivotal. Study EFC5722 was a 12-week, double-blind, randomized, placebo-controlled, parallel-group, multicenter, multinational, efficacy, pharmacodynamic and safety study of two doses of alfuzosin in pediatric patients, age 2-16 years, with elevated detrusor leak point pressure ($\geq$ 40 cm H_2O) of neurologic origin. A brief summary of Study EFC5722 is presented in Table 2.1 below and is the focus of this review.

Table 2.1
Summary of Pivotal Study EFC5722

Study	Study Country (No. of Centers)	Study Design	Number Randomized by Treatment Group	Duration of Treatment
Study EFC5722	Canada (1), Estonia (1), France (3), Germany (2), India (4), Malaysia (1), Poland (6), Portugal (3), Russia (5), Serbia & Montenegro (3), Slovakia (2), Spain (5), Taiwan (2), Turkey (4), US (7)	Randomized, Double-blind, Placebo-controlled, Multicenter, Multinational	Placebo: 57 Alfuzosin 0.1 mg/kg/day: 57 Alfuzosin 0.2 mg/kg/day: 58	12-week treatment phase followed by a 40-week safety extension phase

Source: Reviewer's listing

2.2 Data Sources

The study report and additional information were submitted electronically. The data quality was limits. The analysis datasets and associated definition files are listed in Table 2.2.

Table 2.2
Study EFC5722: Data Sources

Study	File	Location
Study EFC5722	Datasets	\\CDSESUB1\EVSPROD\NDA021287\0015\m5\datasets\efc5722\analysis\
	Definition	\\CDSESUB1\EVSPROD\NDA021287\0015\m5\datasets\efc5722\analysis\define.pdf

2.3 Indication

Alfuzosin is indicated for the treatment of pediatric patients aged 2 to 16 years with elevated leak point pressure associated with a known neurological disorder.

3. STATISTICAL EVALUATION

3.1 Overview of Study EFC5722

3.1.1 Design and Objectives

Design: Study EFC5722 was a randomized, double-blind, placebo-controlled, parallel-group, multicenter, multinational trial. It was conducted in 49 sites across 15 countries (see Table 2.1). The objective of this study was to establish the efficacy of two alfuzosin doses compared to placebo for reducing the detrusor leak point pressure (LPP) in children and adolescents aged 2-16 with elevated detrusor LPP of neuropathic etiology and detrusor LPP $\geq$ 40 cm H_2O.

Approximately 150 patients were planned to be randomized in a 2:1:2:1 ratio to one of four treatment groups:

- oral 0.1 mg/kg/day alfuzosin
- matching placebo for 0.1 mg/kg/day alfuzosin
- oral 0.2 mg/kg/day alfuzosin
- matching placebo for 0.2 mg/kg/day alfuzosin

This resulted in 50 subjects per treatment when both placebo groups are combined.

Randomization was centrally controlled via an interactive voice response system and was stratified by three factors: age (2-7 and 8-16 years of age), pre-existing usage of anticholinergic and/or antimuscarinic drugs, and formulation (tablet or oral solution). Following randomization, children aged 2-7 received alfuzosin oral solution TID close to their three mealtimes (breakfast, lunch, and dinner) and children aged 8-16 received alfuzosin tablets BID approximately every 12 hours. There was a 12-week double-blind efficacy phase followed by a 40-week open-label safety extension phase with a 1 week follow-up at the end of each of the two study phases.

Primary Efficacy Endpoints: The primary efficacy endpoint was the proportion of patients with detrusor LPP < 40 cm H_2O (response) at Week 12.

Secondary Efficacy Endpoints: There were five secondary efficacy endpoints:

- the absolute change in detrusor LPP at Week 12
- the relative change in detrusor LPP at Week 12
- the relative change in detrusor compliance at Week 12
- average monthly number of urinary tract infection (UTI) episodes during the treatment period
- analyses of patients whose post-treatment LPP < 40 cm H_2O with a baseline LPP between 41-45 cm H_2O

Labeling claims are not being sought for these secondary efficacy endpoints.

Determination of Sample Size: The assumptions for sample size calculation were:

- 50% of patients in the alfuzosin group would have a detrusor LPP < 40 cm H_2O at Week 12
- 10% of patients in the placebo group would have a detrusor LPP < 40 cm H_2O at Week 12
- 15% rate of missing LPP data at Week 12

A total of 150 patients (50 patients per treatment group) would provide approximately 95% power to detect a 40% difference in response rate between each alfuzosin dose and placebo at an alpha level of 0.025.

Definition of Analysis Sets (Population): The intent-to-treat (ITT) population was the primary efficacy population. The ITT population included all randomized patients who had at least one post-baseline value and an appropriate baseline value.

The per-protocol (PP) population included all ITT patients with no major efficacy-related protocol deviations. The PP population analysis was performed only if at least 5% of the ITT population was excluded in the PP population. The safety population included all randomized patients who were exposed to the study medication.

Handling of Missing Data: For the primary analysis, patients without post-baseline LPP assessment were considered treatment failures.

Statistical Methods: For LPP assessment, the proportions of patients with LPP < 40 cm H_2O in both doses of alfuzosin were compared to that in the placebo group using Fisher's exact test. The overall type-1 error is controlled at 0.05 using the Hochberg procedure to adjust for multiple comparisons to placebo.

For the secondary analyses, an ANCOVA model was used for the absolute and relative changes in detrusor LPP from baseline. The ANCOVA model included the centered baseline detrusor LPP as covariate and fixed effect of treatment, age/formulation group and previous anticholinergic/antimuscarinic use (Y/N). If the normality assumption was not met, a ranked ANCOVA would be performed.

3.2 Results: Study EFC5722

3.2.1 Subject Disposition

Table 3.2.1 presents the subject disposition. A total of 172 subjects were randomized at 49 sites across 15 countries. All sites recruited less than 20 subjects with 13 sites recruiting 1 subject and 4 sites recruiting at least 10 subjects. Overall, 2.9% of subjects discontinued the study, mostly due to adverse events (2.3%). The discontinuation rates were similar across the three treatment groups. The ITT population of 172 subjects is greater than the planned 150 subjects.

Table 3.2.1 Study EFC5722: Disposition of Subjects During Double-blind Period				
Category	**Placebo N=57**	**Alfuzosin (mg/kg/day)**		**Total N=172**
		0.1 N=57	**0.2 N=58**	
Randomized (ITT)	57 (100%)	57 (100%)	58 (100%)	172 (100%)
Completed Treatment Period	56 (98.2%)	55 (96.5%)	56 (96.6%)	167 (97.1%)
Continued in Open Label Period	54 (94.7%)	54 (94.7%)	55 (94.8%)	163 (94.8%)
Completed both Periods				
Discontinued Treatment Period				
Adverse Event	1 (1.8%)	1 (1.8%)	2 (3.4%)	4 (2.3%)
Lack of Efficacy	0	0	0	0
Lost to follow-up	0	0	0	0
Poor Compliance to Protocol	0	0	0	0
Other Reason	0	1 (1.8%)*	0	1 (0.6%)
ITT Population	57	57	58	172
Per Protocol Population	50	49	50	149
Safety population	57	57	58	172
Source: Reviewer's analysis on Datasets ADDS and ADSL *: Too many blood draws. Child was not better with treatment.				

3.2.2 Patient Demographics and Baseline Characteristics

The patient demographic characteristics are presented in Table 3.2.2. Patients were similar among the three treatment groups in terms of age, body mess index (BMI) and sex. However, for race, there were more Asian patients in each of the two alfuzosin groups compared to placebo. This imbalance was investigated further in the geographic region subgroup analysis.

Table 3.2.2 Study EFC5722: Subject Demographic Summary (ITT Population)				
	Placebo N=57	Alfuzosin		Total N=172
		0.1 mg/kg/day N=57	0.2 mg/kg/day N=58	
Age (SD)	8.3 (4.38)	7.9 (3.91)	8.7 (3.87)	8.3 (4.05)
Body Mass Index (SD)	18.0 (4.58)	18.7 (5.95)	18.8 (4.66)	18.5 (5.09)
Sex:				
Female	28	27	30	85
Male	29	30	28	87
Race [N (%)]				
Caucasian	49 (86.0%)	44 (77.2%)	44 (75.9%)	137 (79.7%)
African American	1 (1.8%)	1 (1.8%)	3 (5.2%)	5 (2.9%)
Asian	5 (8.8%)	11 (19.3%)	10 (17.2%)	26 (15.1%)
Other	2 (3.5%)	1 (1.8%)	1 (1.7%)	4 (2.3%)
Source: Reviewer's analysis				

3.2.3 Primary Efficacy

Table 3.2.3 presents the primary efficacy results. I concur with the sponsor's results. Neither of the two alfuzosin doses demonstrated a statistically greater proportion of patients with a detrusor LPP < 40 cm H_2O at Week 12 compared to placebo. The proportion in each group is as follows: 40.4% in the placebo group, 40.4% in the 0.1 mg/kg/day alfuzosin group, and 48.3% in the 0.2 mg/kg/day alfuzosin group.

Table 3.2.3 Study ECF5722: Proportion of Patients with Detrusor Leak Point Pressure (LPP) < 40 cm H_2O (ITT Population)				
Treatment Group	**N**	**LPP < 40 cm H_2O % (n)**	**Treatment Difference % (95% C.I.)**	**p-value***
Alfuzosin 0.1 mg/kg/day	57	40.4 (23)	0 (-17.48, 17.48)	1.00
Alfuzosin 0.2 mg/kg/day	58	48.3 (28)	7.9 (-9.97, 25.11)	0.91
Placebo	57	40.4 (23)		
Source: Reviewer's analysis * Nominal p-value				

3.3.4 Secondary Efficacy

The absolute change and relative change in LPP from baseline to Week 12 were not significantly reduced in both alfuzosin groups compared to placebo (see Tables A.1 and A.2 in the Appendix). These two secondary efficacy results support the findings from the primary efficacy analysis.

There was no significant benefit found in either of the other secondary endpoints of absolute and relative detrusor compliance at Week 12 and the number of UTI episodes during the treatment period (not shown).

3.3.6 Reviewer's Comments on the Efficacy Results

The two doses of alfuzosin did not demonstrate a statistically significant benefit compared to placebo in the treatment of pediatric patients aged 2 to 16 years with elevated leak point pressure associated with a known neurological disorder. The proportion of patients with detrusor LPP < 40 cm H_2O after 12 weeks of treatment is: 40.4% in the placebo group, 40.4% in the 0.1mg/kg/day group, and 48.3% in the 0.2 mg/kg/day alfuzosin group.

The negative study results may be due to the actual study power being lower than the protocol planned 95% because the placebo effect was larger (40.4%) than what was assumed (10%) for sample size calculation.

Also, the distribution of the change from baseline LPP values did not suggest that a single site influenced efficacy (see Figure A.1 in the Appendix).

3.4 Evaluation of Safety

See the Medical Officer's review for an evaluation of safety.

4. FINDINGS IN SPECIAL/SUBGROUP POPULATIONS

4.1 Age, Gender Region, Formulation, and Anticholinergic/Antimuscarinic Agent Usage

Subgroup analyses by age, race, geographic region, formulation, and pre-existing anticholinergic/antimuscarinic usage for the primary efficacy endpoint, LPP < 40 cm H_2O at Week 12, were requested by the clinical reviewer and are briefly presented in this section. I concur with the sponsor's results. The results tables can be found in the Appendix.

There was no significant difference in the proportion of patients with LPP < 40 cm H_2O in either of the two alfuzosin dose groups compared to placebo for each of the following subgroups:

- Age groups of 2 – 7 years and 8 – 16 years (Table A.3)
- Gender groups of male and female (Table A.4)
- Geographic regions of Asia, Eastern Europe, Western Europe and North America (Table A.5)
- Formulation groups of solution and tablet (Table A.6)
- Pre-existing anticholinergic/antimuscarinic usage groups of user and non-user (Table A.7)

Although there was no significant difference in the proportion of patients with LPP < 40 cm H_2O in either of the two alfuzosin dose groups compared to placebo within the female subgroup analysis, there was a trend in dose effect with proportions of 51.9% and 63.3% in the lower and higher alfuzosin doses, respectively, compared to 39.3% in placebo (Table A.4).

4.3 Reviewer comments on subgroup analysis

We performed exploratory analyses for the subgroups of age, gender, region, formulation and anticholinergic/antimuscarinic usage. Due to small subgroup sizes, the results of these analyses do not demonstrate significant differences in any subgroup for each of the two alfuzosin doses compared to placebo.

5. SUMMARY AND CONCLUSIONS

5.1 Statistical Issues and Collective Evidence

There were no statistical issues in the efficacy evaluation. There was an unexpectedly high placebo response rate seen in this study. The proportion of pediatric patients with detrusor LPP < 40 cm H_2O in the placebo group at Week 12 was 40.4%, greater than the assumed proportion of 10% used for sample size calculation. For comparison, the proportions in both alfuzosin doses are close to the assumed proportion of 50%.

Neither the 0.1 mg/kg/day nor the 0.2 mg/kg/day alfuzosin dose demonstrated efficacy for the treatment of pediatric patients aged 2 to 16 years with elevated leak point pressure (LPP) associated with a known neurological disorder based on the proportion of patients with detrusor LLP < 40 cm H_2O. Descriptively, the proportion of patients with detrusor LLP < 40 cm H_2O was 48.3% in the 0.2 mg/kg/day alfuzosin group, 40.4% in the 0.1 mg/kg/day alfuzosin group, and 40.4% in the placebo group.

5.2 Conclusions and Recommendations

From a statistical perspective, the data from a study conducted under a Pediatric Written Request do not support either the 0.1 mg/kg/day or 0.2 mg/kg/day alfuzosin dose for the treatment of pediatric patients aged 2 to 16 years with elevated leak point pressure (LPP) associated with a known neurological disorder based on the proportion of patients with detrusor LLP < 40 cm H_2O. Descriptively, the proportion of patients with detrusor LLP < 40 cm H_2O was 48.3% in the 0.2 mg/kg/day alfuzosin group, 40.4% in the 0.1 mg/kg/day alfuzosin group, and 40.4% in the placebo group.

Appendix: Figures and Tables

Figure A.1: Mean Change from Baseline LPP by Study Site

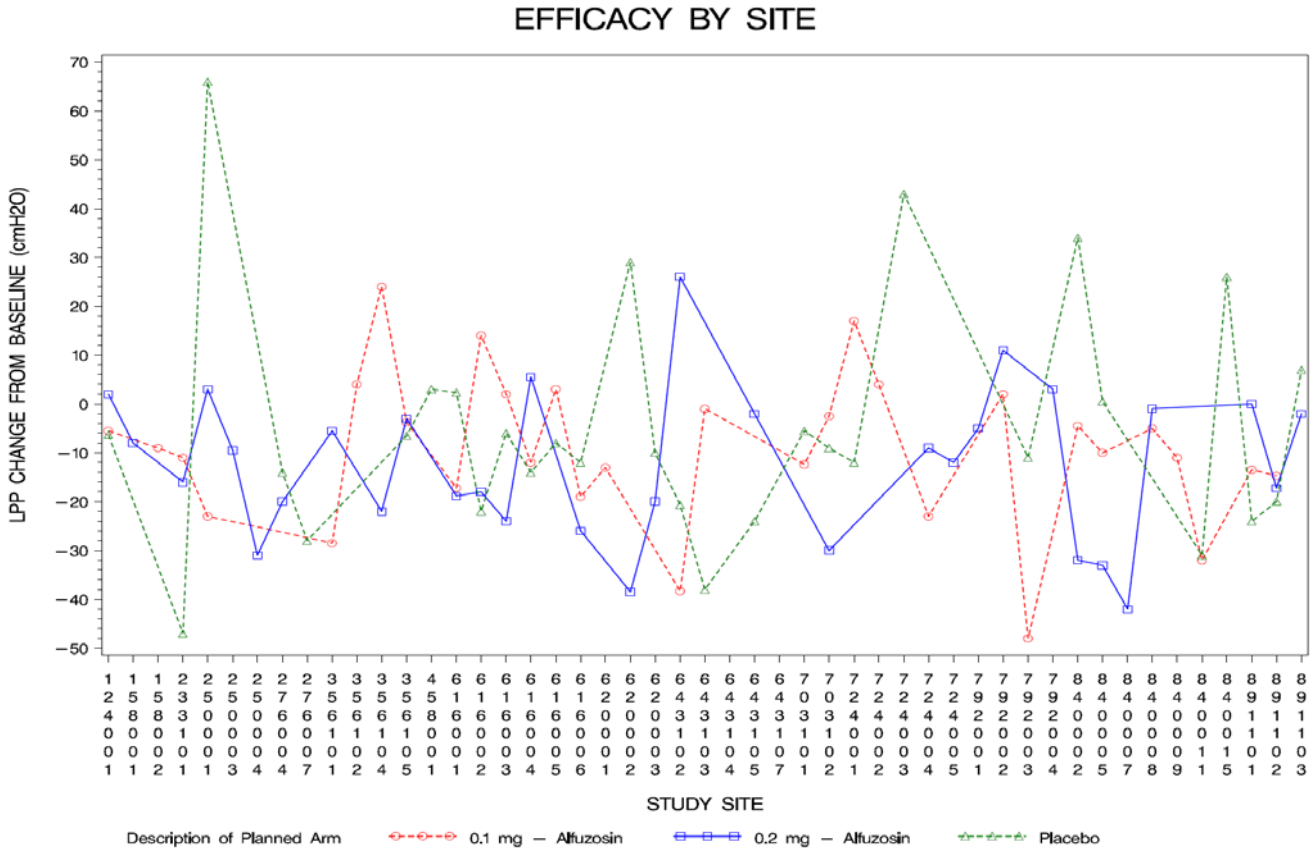

Table A.1 Absolute Change in LPP from Baseline to Week 12 (ITT Population)				
Treatment Group	**N**	**LPP ($cm H_2O$)**	**Treatment Difference (95% C.I.)**	**p-value***
Alfuzosin 0.1 mg/kg/day	57	-11.6	-6.2 (-13.7, 1.31)	0.105
Alfuzosin 0.2 mg/kg/day	58	-12.5	-7.0 (-14.5, 0.4)	0.064
Placebo	57	-5.4		

Source: Reviewer's analysis
* Nominal p-value based on an ANCOVA model with fixed effect of treatment, age, formulation, anticholinergic/antimuscarinic use and baseline as covariate.

Table A.2
Relative Change of LPP from Baseline to Week 12 (ITT Population)

Treatment Group	N	LPP (%)	Treatment Difference (95% C.I.)	p-value*
Alfuzosin 0.1 mg/kg/day	57	-20.6%	-11.4% (-26.3%, 3.5%)	0.132
Alfuzosin 0.2 mg/kg/day	58	-23.5%	-14.3% (-29.1%, 0.5%)	0.059
Placebo	57	-9.2		

Source: Reviewer's analysis
* Nominal p-value based on an ANCOVA model with fixed effect of treatment, age, formulation, anticholinergic/antimuscarinic use and baseline as covariate.

Table A.3
Study ECF5722: Age Subgroup Analysis for Primary Efficacy Endpoint of Proportion of Patients with Detrusor Leak Point Pressure (LPP) < 40 cm H_2O (ITT Population)

Age Group	Treatment	N	LPP < 40 cm H_2O % (n)	Treatment Difference % (95% C.I.)	p-value*
2 – 7 Years	Alfuzosin 0.1 mg/kg/day	28	53.6 (15)	21.4 (-4.2, 43.5)	0.11
	Alfuzosin 0.2 mg/kg/day	28	46.4 (13)	14.3 (-10.8, 37.0)	0.27
	Placebo	28	32.1 (9)		
8 - 16 Years	Alfuzosin 0.1 mg/kg/day	29	27.6 (8)	-20.7 (-42.3, 4.1)	0.10
	Alfuzosin 0.2 mg/kg/day	30	50.0 (15)	1.7 (-22.4, 25.6)	0.90
	Placebo	29	48.3 (14)		

Source: Reviewer's analysis
* Nominal p-value

Table A.4
Study ECF5722: Gender Subgroup Analysis for Primary Efficacy Endpoint of Proportion of Patients with Detrusor Leak Point Pressure (LPP) < 40 cm H_2O (ITT Population)

Gender Group	Treatment	N	LPP < 40 cm H_2O % (n)	Treatment Difference % (95% C.I.)	p-value*
Female	Alfuzosin 0.1 mg/kg/day	27	51.9 (14)	12.6% (-13.0%, 36.0%)	0.350
	Alfuzosin 0.2 mg/kg/day	30	63.3 (19)	24.5% (-1.5%, 45.6%)	0.067
	Placebo	28	39.3 (11)		
Male	Alfuzosin 0.1 mg/kg/day	30	30.0 (9)	-11.4% (-33.7%, 12.5%)	0.361
	Alfuzosin 0.2 mg/kg/day	28	32.1 (9)	-9.2% (-32.1%, 15.1%)	0.470
	Placebo	29	41.4 (12)		

Source: Reviewer's analysis
* Nominal p-value

Table A.5
Study ECF5722: Region Subgroup Analysis for Primary Efficacy Endpoint of Proportion of Patients with Detrusor Leak Point Pressure (LPP) < 40 cm H_2O (ITT Population)

Region Group	Treatment	N	LPP < 40 cm H_2O % (n)	Treatment Difference % (95% C.I.)	p-value*
Asia	Alfuzosin 0.1 mg/kg/day	10	30.0 (3)	10.0% (-36.6%, 44.5%)	1.000 [a]
	Alfuzosin 0.2 mg/kg/day	10	20.0 (2)	0.0% (-44.8%, 35.0%)	1.000 [a]
	Placebo	5	20.0 (1)		
Eastern Europe	Alfuzosin 0.1 mg/kg/day	33	48.5 (16)	2.8% (-19.9%, 25.1%)	0.819
	Alfuzosin 0.2 mg/kg/day	30	46.7 (14)	1.0% (-22.1%, 23.9%)	0.939
	Placebo	35	45.7 (16)		
Western Europe and North America	Alfuzosin 0.1 mg/kg/day	14	28.6 (4)	-6.7% (-35.6%, 25.0%)	0.690
	Alfuzosin 0.2 mg/kg/day	18	66.7 (12)	31.3% (-1.4%, 56.2%)	0.063
	Placebo	17	35.3 (6)		

Source: Reviewer's analysis
* Nominal p-value
a: from Fisher Exact Test

Table A.6
Study ECF5722: Formulation Subgroup Analysis for Primary Efficacy Endpoint of Proportion of Patients with Detrusor Leak Point Pressure (LPP) < 40 cm H_2O (ITT Population)

Formulation Group	Treatment	N	LPP < 40 cm H_2O % (n)	Treatment Difference % (95% C.I.)	p-value*
Solution	Alfuzosin 0.1 mg/kg/day	38	44.7 (17)	8.6% (-0.13.3%, 8.6%)	0.450
	Alfuzosin 0.2 mg/kg/day	37	48.7 (18)	12.5% (-9.8%, 33.1%)	0.279
	Placebo	36	36.1 (13)		
Tablet	Alfuzosin 0.1 mg/kg/day	19	31.6 (6)	-16.0% (-41.8%, 13.5%)	0.301
	Alfuzosin 0.2 mg/kg/day	21	47.6 (10)	0.0% (-27.8%, 27.8%)	1.000
	Placebo	21	47.6 (10)		

Source: Reviewer's analysis
* Nominal p-value

Table A.7
Study ECF5722: Anticholinergic/Antimuscarinic Subgroup Analysis for Primary Efficacy Endpoint of Proportion of Patients with Detrusor Leak Point Pressure (LPP) < 40 cm H_2O (ITT Population)

Anticholinergic/ antimuscarinic	Treatment	N	LPP < 40 cm H_2O % (n)	Treatment Difference % (95% C.I.)	p-value*
User	Alfuzosin 0.1 mg/kg/day	31	41.9 (13)	2.6% (-21.3%, 26.0%)	0.836
	Alfuzosin 0.2 mg/kg/day	32	53.1 (17)	13.8% (-10.9%, 36.3%)	0.284
	Placebo	28	39.3 (11)		
Non User	Alfuzosin 0.1 mg/kg/day	26	38.5 (10)	-2.9% (-26.9%, 21.8%)	0.826
	Alfuzosin 0.2 mg/kg/day	26	42.3 (11)	0.9% (-23.6, 25.5%)	0.944
	Placebo	29	41.4 (12)		

Source: Reviewer's analysis
* Nominal p-value

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

XIN FANG
11/26/2010

SONIA CASTILLO
11/26/2010
Signing off for Mahboob Sobhan