U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Pharmacoepidemiology and Statistical Science
Office of Biostatistics

STATISTICAL REVIEW AND EVALUATION

CLINICAL STUDIES

NDA/Serial Number:	20-408 / S-033
Drug Name:	TRUSOPT (Dorzolamide Hydrochloride) Ophthalmic Solution 2.0%
Indication(s):	The treatment of elevated intraocular pressure in patients with ocular hypertension or open angle glaucoma
Applicant:	Merck & Co., Inc.
Date(s):	Submitted: October 16, 2003 Received: October 16, 2003
Review Priority:	Priority review
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Keywords: Pediatric exclusivity, Confidence interval (for binomial proportion), Endpoint analysis with LOCF

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1. EXECUTIVE SUMMARY

1.1 Conclusions and Recommendations

Based on the data from this pediatric study for marketing exclusivity extension, we conclude that dorzolamide ophthalmic solution resulted in significant reduction of intraocular pressure (IOP) 'after treatment' compared with 'before treatment' in pediatric patients with glaucoma of age less than 6. Also, it appears that the proportion of discontinuation of therapy due to a drug-related adverse experience was within prespecified limits.

1.2 Brief Overview of Clinical Study

The sponsor submitted the results of a study that documents the efficacy and safety of dorzolamide hydrochloride in pediatric patients less than six years of age with a clinical diagnosis of glaucoma or elevated intraocular pressure. This single study was a combination of two identical protocols (Protocols 100 and 125) for U.S. and international sites, respectively. This was a **3-month**, double-masked, active-treatment-controlled, multicenter study to investigate the safety and ocular hypotensive effect of **dorzolamide 2% sterile solution** 3 times a day in pediatric glaucoma patients younger than 6 years of age. Timolol maleate gel-forming solution once daily was the active treatment control.

83 patients younger than 2 years of age were randomized to the dorzolamide arm (n = 56) and the timolol GS arm (n = 27) in 2-to-1 ratio. 101 patients ≥ 2 years but < 6 years of age were randomized to the dorzolamide arm (n = 66) and the timolol GS arm (n = 35) in 2-to-1 ratio.

The primary objective of the study was to document an acceptable safety profile for initial therapy with dorzolamide. The primary measure of safety was the proportion of patients who discontinue therapy due to a drug-related adverse experience prior to completing 3 months of therapy.

The secondary objective was to characterize the IOP-lowering effect of dorzolamide. The primary efficacy endpoint was the intraocular pressure change from baseline and percent change from baseline at the end-of-study (Week 12) visit.

Statistical data analyses and presentation were done by age cohort and in all combined patients.

1.3 Statistical Issues and Findings

For the efficacy analysis, the sponsor focused on the statistical significance of decrease in IOP 'before and after' dorzolamide treatment without comparing the decrease with that of the active comparator, timolol.

The comparisons in efficacy between dorzolamide and timolol groups were done using a confidence interval method in a post hoc manner instead of a pre-planned statistical hypothesis testing method. While 95% confidence intervals of difference in IOP decrease after treatment between dorzolamide and timolol included zero indicating that the effect of dorzolamide was not statistically different from that of timolol, a clinical judgment is required regarding similarity in efficacy between the two treatments by assessing the width of the confidence interval.

The safety endpoint was not compared between treatment groups, but was evaluated only within dorzolamide group although the clinical trial was controlled with active comparator.

Based on our review of the data up to 12 weeks we conclude the following:

1. The 95% confidence intervals for the proportion of discontinuation of therapy due to a drug-related adverse experience for dorzolamide group were (0.05%, 9.55%) for age-cohort < 2 years of age and (0.37%, 10.52%) for age-cohort ≥2 years but <6 years of age. Therefore, the safety of dorzolamide in both age-cohorts was shown according to the pre-defined decision rule, which claims the safety if the upper limit is lower than 25%.

2. At Week 12 for age-cohort <2 years of age, there were statistically significant decreases from baseline in IOP in both treatment groups and the decrease were similar in the dorzolamide and timolol groups with mean change changes from baseline (95% CI) in IOP of -7.30 (-9.51, -5.03) vs. -7.80 (-10.90, -4.74) mm Hg. The difference between the two treatments and the 95% CI for the difference were 0.57 (-3.39, 4.54) mm Hg, indicating a similar effect for the two treatment groups.

3. At Week 12 for age-cohort ≥2 years but <6 years of age, there were statistically significant decreases from baseline in IOP in both treatment groups and the decrease were similar in the dorzolamide and timolol groups with mean change changes from baseline (95% CI) in IOP of -7.10 (-8.72, -5.39) vs. -7.40 (-9.67, -5.13) mm Hg. The difference between the two treatments and the 95% CI for the difference were 0.34 (-2.50, 3.19) mm Hg, indicating a similar effect for the two treatment groups.

4. At Week 12 for age-cohorts combined, there were statistically significant decreases from baseline in IOP in both treatment groups and the decrease were similar in the

dorzolamide and timolol groups with mean change changes from baseline (95% CI) in IOP of -7.20 (-8.53, -5.79) vs. -7.60 (-9.45, -5.75) mm Hg. The difference between the two treatments and the 95% CI for the difference were 0.44 (-1.92, 2.79) mm Hg, indicating a similar effect for the two treatment groups.

2. INTRODUCTION

2.1 Overview

2.1.1 Drug class and regulatory history

Dorzolamide, which was approved in 1994, was the first topical carbonic anhydrase inhibitor approved for use in the United States to treat glaucoma.

The FDA has issued a written request for a pediatric study of dorzolamide in June 1999, and amended in May 2000 and February 2002. In the Written Request, the FDA specified that a randomized, double-masked, parallel-comparison study with a minimum 50 patients <2 years of age and a minimum of 50 patients 2 to 5 years of age randomized to dorzolamide monotherapy be conducted.

2.1.2 Indication for TRUSOPT™ (dorzolamide)

TRUSOPT Ophthalmic Solution is indicated in the treatment of elevated IOP in patients with ocular hypertension or open-angle glaucoma. The dosing recommended by the sponsor is one drop of TRUSOPT Ophthalmic Solution in the affected eye(s) three times daily.

2.2 Data Sources

The original electronic submission on October 16, 2003 can be found on the FDA, CDER electronic document room (EDR).

Final Report:
\\Cdsesub1\n20408\S_033\2003-10-16\clinstat\studies

Data set:
\\Cdsesub1\n20408\S_033\2003-10-16\crt\datasets

3. STATISTICAL EVALUATION

3.1 Evaluation of Efficacy

3.1.1 Study Design and Endpoints

This was a 3-month, double-masked, active-treatment-controlled, multicenter study to investigate ocular hypotensive effect of dorzolamide 2% t.i.d. in pediatric glaucoma patients younger than 6 years. Timolol maleate gel-forming solution (timolol GS) q.d. was the active treatment control. Patients were randomized 2:1, dorzolamide to timolol GS therapy. If IOP was inadequately controlled on monotherapy, a change was made to open-label concomitant therapy of dorzolamide 2% t.i.d. and timolol GS 0.25% q.d. for patients <2 years of age or combination therapy of dorzolamide 2%/ timolol 0.5% b.i.d. for patients ≥2 years but <6 years of age. Figure 1 shows a schematic of the study design of Protocols 100 and 125 in two age cohorts and Table 1 shows change in therapy schedule.

Figure 1. Schematic of Study Design

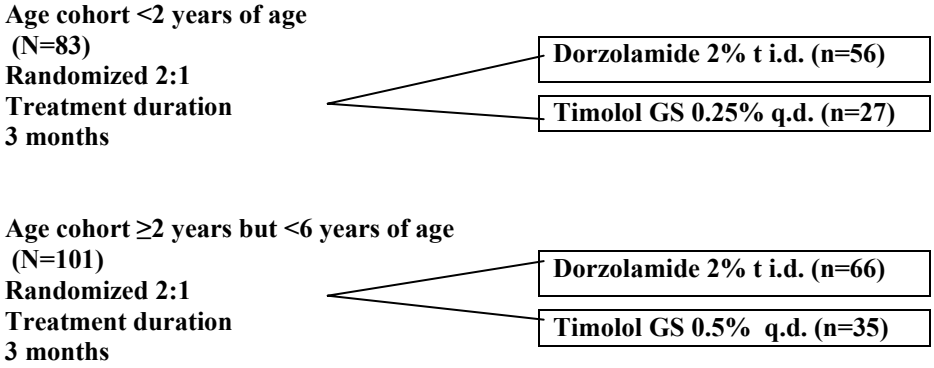

Table 1. Change in Therapy Schedule

Patient Age	Initial Therapy (Masked)	Concomitant/Combination Therapy (Open Label)
<2 years	Dorzolamide 2% t.i.d. Or Timolol GS 0.25% q.d.	Dorzolamide 2% t.i.d. plus Timolol GS 0.25% q.d.
≥2 years but <6 years	Dorzolamide 2% t.i.d. Or Timolol GS 0.5% q.d.	Dorzolamide 2%/ Timolol GS 0.5% fixed combination b.i.d.

The study was an international one. The distribution of the centers by country is as follows:

Protocol 100: USA(22)
Protocol 125: Mexico(1), Philippine(1), Columbia(2), Poland(1), Venezuela(2), Egypt(1), Czech Republic(2), Croatia(1), Peru(1), Guatemala(1).

IOP as efficacy outcome was measured on Study Day 1, and Weeks 1, 4, and 12, and at Weeks 2 or 5 if a change in therapy is implemented. The primary efficacy endpoint was the intraocular pressure change from baseline and percent change from baseline at the end-of-study (Week 12) visit. IOP change from baseline and percent change from baseline were tested at each post baseline visit within dorzolamide treatment group using paired t test.

3.1.2 Patient Disposition, Demographic and Baseline Characteristics

As shown in Table 2 below, about 10% of the patients did not complete the study. For the missing data due to discontinuation, LOCF was used in the efficacy analysis.

Table 2. Patient Disposition

AGE COHORT	<2 Years		≥2 Years but <6 Years		TOTAL
SCREENING FAILURES:	13		19		32
TREATMENT GROUP:	Dorzolamide 2%	Timolol GS 0.25%	Dorzolamide 2%	Timolol GS 0.5%	
RANDOMIZED:	56	27	66	35	184
Masked Monotherapy Phase					
COMPLETED:	28	16	41	21	106
DISCONTINUED:	6	3	4	3	18
Lost to follow-up	1	0	0	0	1
Withdrew consent	0	0	1	0	1
Clinical adverse experience	0	2	2	2	6
IOP not controlled-surgery	4	0	3	1	8
IOP not controlled-medication	0	1	0	0	1
Other reason	1	0	0	0	1
Patient switched to open-label concomitant therapy	22	8	19	11	60

Open-Label Concomitant Therapy Phase					
COMPLETED:	15	7	12	7	41
DISCONTINUED:	7	1	7	4	19
IOP not controlled-surgery	5	1	5	2	13
IOP not controlled-medication	1	0	2	1	4
Other reason	1	0	0	1	
Overall					
COMPLETED:	43	23	53	28	147
DISCONTINUED:	13	4	13	7	37
Lost to follow-up	1	0	0	0	1
Withdrew consent	0	0	1	0	1
Clinical adverse experience	0	2	2	2	6
IOP not controlled-surgery	9	1	8	3	21
IOP not controlled-medication	1	1	2	1	5
Other	2	0	0	1	3

Table 3 and Table 4 below show patient demographics and baseline characteristics by treatment groups, respectively.

Table 3. Patient Demographics

AGE COHORT	<2 Years		≥2 Years but <6 Years		Combined	
TREATMENT GROUP:	Dorzolamide 2%	Timolol GS 0.25%	Dorzolamide 2%	Timolol GS 0.5%	Dorzolamide 2%	Timolol GS 0.25% and 0.5%
N:	56	27	66	35	122	62
Gender						
Male	35 (62.5%)	20 (74.1%)	33 (50%)	18 (51.4%)	68 (55.7%)	38 (61.3%)
Female	21 (37.5%)	7 (25.9%)	33 (50%)	17 (48.6%)	54 (44.3%)	24 (38.7%)
Race						
Asian	5 (8.9%)	2 (7.4%)	5 (7.6%)	2 (5.7%)	10 (8.2%)	4 (6.5%)
Bi-Racial	1 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Black	4 (7.1%)	2 (7.4%)	4 (6.1%)	1 (2.9%)	8 (6.6%)	3 (4.8%)
Caucasian	16 (28.6%)	7 (25.9%)	23 (34.8%)	14 (40.0%)	39 (32%)	21 (33.9%)
Egyptian	8 (14.3%)	4 (14.8%)	8 (12.1%)	4 (11.4%)	16 (13.1%)	8 (12.9%)
Hispanic	22 (39.3%)	11 (40.7%)	26 (39.4%)	12 (34.3%)	48 (39.3%)	23 (37.1%)
Hispanic/White	0 (0.0%)	1 (3.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.6%)
Indian	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (5.7%)	0 (0.0%)	2 (3.2%)

Age	**(Months)**		**(Years)**		**(Months)**	
Mean	9.7	11.5	3.4	3.5	29.8	32.2
SD	6.5	6.4	1.2	1.2	21.9	22.2
Median	8	11	3	3	27	29.5
Range	1 to 23	0.25 to 22	2 to 6	2 to 6	1 to 77	0.25 to 83

Table 4. Baseline Characteristics

AGE COHORT	<2 Years		≥2 Years but <6 Years		Combined	
TREATMENT GROUP:	Dorzolamide 2%	Timolol GS 0.25%	Dorzolamide 2%	Timolol GS 0.5%	Dorzolamide 2%	Timolol GS 0.25% and 0.5%
N	56	27	66	35	122	62
Baseline IOP (mmHg) – Worse Eye						
Mean	32.6	29.9	28.7	30.3	30.5	30.1
SD	11.1	8.6	7.4	6.5	9.5	7.4
Median	29	28	26	30	27	29.5
Range	17.3 to 64	14 to 48.7	18 to 55	22 to 45.5	17.3 to 64	14 to 48.7

3.1.3 Statistical Methodologies

Sponsor employed the paired t test to compare 'before' and 'after' treatment IOP measurements. Reviewer did the same analysis adjusting for regional effects (US and non-US) using an analysis of variance (ANOVA) with terms of patient, week, and region. But the re-analyses resulted in the similar p-values for the efficacy comparison as those provided by the sponsor.

3.1.4 Results and Conclusions

Table 5 – Table 7 present the statistical analyses done by sponsor except for the p-values which were recalculated by the reviewer in order to adjust for regional effect.

At Week 12 for age-cohort <2 years of age, there were statistically significant decreases from baseline in IOP in both treatment groups and the decrease were similar in the dorzolamide and timolol groups with mean change changes from baseline (95% CI) in IOP of -7.30 (-9.51, -5.03) vs. -7.80 (-10.90, -4.74) mm Hg. The difference between the two treatments and the 95% CI for the difference were 0.57 (-3.39, 4.54) mm Hg, indicating that the effect of dorzolamide was not statistically different from that of timolol.

At Week 12 for age-cohort ≥2 years but <6 years of age, there were statistically significant decreases from baseline in IOP in both treatment groups and the decrease were similar in the dorzolamide and timolol groups with mean change changes from

baseline (95% CI) in IOP of -7.10 (-8.72, -5.39) vs. -7.40 (-9.67, -5.13) mm Hg. The difference between the two treatments and the 95% CI for the difference were 0.34 (-2.50, 3.19) mm Hg, indicating that the effect of dorzolamide was not statistically different from that of timolol.

At Week 12 for age-cohorts combined, there were statistically significant decreases from baseline in IOP in both treatment groups and the decrease were similar in the dorzolamide and timolol groups with mean change changes from baseline (95% CI) in IOP of -7.20 (-8.53, -5.79) vs. -7.60 (-9.45, -5.75) mm Hg. The difference between the two treatments and the 95% CI for the difference were 0.44 (-1.92, 2.79) mm Hg, indicating that the effect of dorzolamide was not statistically different from that of timolol.

Basically, the sponsor calculated the mean IOP change from baseline and percent change from baseline and tested if these were statistically different from zero. Statistical comparisons were not done between treatment groups. But the sponsor provided the differences between the treatment groups and the 95% confidence intervals, which gave some idea regarding similarity of the IOP between the two treatment groups although it was not clearly stated in the protocol. Therefore, even if the sponsor provided a partial evidence regarding the similarity in IOP lowering effect between the two treatments, the sponsor cannot claim that dorzolamide is similarly effective when compared with the active comparator timolol GS. This claim can be shown by a pre-planned equivalence trial with appropriate equivalence margin.

Table 5. Analysis Results of IOP (mm Hg) (Age Cohort <2 Years - Monotherapy): ITT and LOCF

Visit	Treatment	N	Baseline outcome		Study outcome		Change		% Change (p-Value)
			Mean	SD	Mean	SD	Mean (p-Value)	SD	
Week 1	Dorzolamide 2%	46	34.07	11.61	31.50	24.05	-10.0 (<0.001)	10.77	-27.4 (<0.001)
	Timolol GS 0.25%	22	31.15	9.02	23.15	8.19	-8.0(<0.001)	8.24	-23.8 (<0.001)
Week 4	Dorzolamide 2%	53	33.16	11.29	24.30	9.58	-8.9(<0.001)	8.15	-25.7 (<0.001)
	Timolol GS 0.25%	24	30.26	8.98	22.67	7.75	-7.6(<0.001)	8.11	-23.8 (<0.001)
Week 12	Dorzolamide 2%	58	32.60	11.03	25.33	9.38	-7.3(<0.001) (-9.51, -5.03)	8.69	-20.6 (<0.001) (-26.3, -15.0)
	Timolol GS 0.25%	27	29.88	8.59	22.03	7.32	-7.8(<0.001) (-10.9, -4.74)	8.23	-24.9 (<0.001) (-32.7, -17.2)
Difference at Week 12: Dorzolamide – Timolol (95% CI)							0.57 (-3.39, 4.54)		4.30 (-5.66, 14.26)

Note: p-Values were based on the ANOVA model with terms of region (US and non-US), patient, and week.
The ITT population consists of all randomized patients that have a baseline value and at least one efficacy measurement subsequent to at least one dose of study therapy during the double-masked phase of the study.

Table 6. Analysis Results of IOP (mm Hg) (Age Cohort ≥2 Years but <6 Years - Monotherapy): ITT and LOCF

Visit	Treatment	N	Baseline outcome		Study outcome		Change		% Change (p-Value)
			Mean	SD	Mean	SD	Mean (p-Value)	SD	
Week 1	Dorzolamide 2%	59	28.49	7.40	21.32	7.95	-7.2 (<0.001)	5.97	-24.8 (<0.001)
	Timolol GS 0.5%	29	30.26	6.76	22.19	7.57	-8.1(<0.001)	7.03	-26.3 (<0.001)
Week 4	Dorzolamide 2%	60	28.22	6.81	20.96	6.31	-7.3(<0.001)	6.26	-24.5 (<0.001)
	Timolol GS 0.5%	30	30.16	6.63	21.97	7.09	-8.2(<0.001)	4.22	-28.0 (<0.001)
Week 12	Dorzolamide 2%	63	28.54	7.49	21.49	6.78	-7.1(<0.001) (-8.72, -5.39)	6.74	-23.3 (<0.001) (-28.9, -17.8)
	Timolol GS 0.5%	34	30.25	6.61	22.85	8.97	-7.4(<0.001) (-9.67, -5.13)	6.74	-25.3 (<0.001) (-33.2, -17.4)
Difference at Week 12: Dorzolamide – Timolol (95% CI)							0.34 (-2.50, 3.19)		1.95 (-7.71, 11.62)

Note: p-Values were based on the ANOVA model with terms of region (US and non-US), patient, and week.
The ITT population consists of all randomized patients that have a baseline value and at least one efficacy measurement subsequent to at least one dose of study therapy during the double-masked phase of the study.

Table 7. Analysis Results of IOP (mm Hg) at Week 12 (Age Cohorts Combined - Monotherapy): ITT and LOCF

Visit	Treatment	N	Baseline outcome		Study outcome		Change		% Change (p-Value)
			Mean	SD	Mean	SD	Mean (p-Value)	SD	
Week 12	Dorzolamide 2%	121	30.49	9.53	23.33	8.32	-7.2(<0.001) (-8.53, -5.79)	7.70	-22.0 (<0.001) (-26.0, -18.1)
	Timolol GS (0.25% or 0.5%)	61	30.08	7.49	22.49	8.22	-7.6(<0.001) (-9.45, -5.75)	7.38	-25.1 (<0.001) (-30.7, -19.6)
Difference at Week 12: Dorzolamide – Timolol (95% CI)							0.44 (-1.92, 2.79)		3.09 (-3.77, 9.95)

Note: p-Values were based on the ANOVA model with terms of region (US and non-US), patient, and week.
The ITT population consists of all randomized patients that have a baseline value and at least one efficacy measurement subsequent to at least one dose of study therapy during the double-masked phase of the study.

3.2 Evaluation of Safety

Safety analyses were based on the All-Patients-as-Treated analysis population, which included all patients who were randomized to double-masked therapy and received at least one dose of study therapy.

3.2.1 Evaluation of Safety (Age Cohort <2 Years Old)

One patient (1.79%, 95% CI [0.05%, 9.55%]) initially randomized to dorzolamide 2% monotherapy discontinued therapy due to a drug-related clinical adverse experience. No patients (0.00%) initially randomized to timolol GS 0.25% monotherapy discontinued therapy due to a drug-related clinical adverse experience.

3.2.2 Evaluation of Safety (Age Cohort ≥2 Years Old but <6 Years Old)

Three (3) patients discontinued therapy due to a drug-related clinical adverse experience: of these 2 patients (3.03%, 95% CI [0.37%, 10.52%]) initially randomized to dorzolamide 2% and 1 patient (2.86%) was initially randomized to timolol GS 0.5%.

3.2.3 Evaluation of Safety (Age Cohorts Combined)

Three (4) patients discontinued therapy due to a drug-related clinical adverse experience: of these 3 patients (2.46%) initially randomized to dorzolamide 2% and 1 patient (1.61%) was initially randomized to timolol GS 0.25% or 0.5%.

3.2.4 Results and Conclusions

The 95% confidence intervals for the proportion of discontinuation of therapy due to a drug-related adverse experience for dorzolamide group were (0.05%, 9.55%) for age-cohort < 2 years of age and (0.37%, 10.52%) for age-cohort ≥2 years but <6 years of age. Therefore, the safety of dorzolamide in both age-cohorts was shown according to the pre-defined decision rule, which claims the safety if the upper limit is lower than 25%.

The proportions of discontinuation of therapy due to a drug-related clinical adverse experience were calculated for each treatment and tested if they were statistically lower than 25% within dorzolamide group using a confidence interval approach.

4. FINDINGS IN SPECIAL/SUBGROUP POPULATIONS

4.1 Gender, Race and Age

Sponsor analyzed data for each of 2 age cohorts: “patients <2 years old” cohort and “patients ≥2 years but <6 years old” cohort.

4.2 Other Special/Subgroup Populations

No further subgroup analyses were performed.

5. SUMMARY AND CONCLUSIONS

5.1 Statistical Issues and Collective Evidence

5.1.1 Statistical Issues

For the efficacy analysis, the sponsor focused on the statistical significance of decrease in IOP 'before and after' dorzolamide treatment without comparing the decrease with that of the active comparator, timolol.

The comparisons in efficacy between dorzolamide and timolol groups were done using a confidence interval method in a post hoc manner instead of a pre-planned statistical hypothesis testing method. While 95% confidence intervals of difference in IOP decrease after treatment between dorzolamide and timolol included zero indicating that the effect of dorzolamide was not statistically different from that of timolol, a clinical judgment is required regarding similarity in efficacy between the two treatments by assessing the width of the confidence interval.

The safety endpoint was not compared between treatment groups, but was evaluated only within dorzolamide group although the clinical trial was controlled with active comparator.

5.1.2 Collective Evidence

Based on our review of the data up to 12 weeks we conclude the following:

1. The 95% confidence intervals for the proportion of discontinuation of therapy due to a drug-related adverse experience for dorzolamide group were (0.05%, 9.55%) for age-cohort < 2 years of age and (0.37%, 10.52%) for age-cohort ≥2 years but <6 years of age. Therefore, the safety of dorzolamide in both age-cohorts was shown according to the pre-defined decision rule, which claims the safety if the upper limit is lower than 25%.

2. At Week 12 for age-cohort <2 years of age, there were statistically significant decreases from baseline in IOP in both treatment groups and the decrease were similar in the dorzolamide and timolol groups with mean change changes from baseline (95% CI) in IOP of -7.30 (-9.51, -5.03) vs. -7.80 (-10.90, -4.74) mm Hg. The

difference between the two treatments and the 95% CI for the difference were 0.57 (-3.39, 4.54) mm Hg, indicating a similar effect for the two treatment groups.

3. At Week 12 for age-cohort ≥2 years but <6 years of age, there were statistically significant decreases from baseline in IOP in both treatment groups and the decrease were similar in the dorzolamide and timolol groups with mean change changes from baseline (95% CI) in IOP of -7.10 (-8.72, -5.39) vs. -7.40 (-9.67, -5.13) mm Hg. The difference between the two treatments and the 95% CI for the difference were 0.34 (-2.50, 3.19) mm Hg, indicating a similar effect for the two treatment groups.

4. At Week 12 for age-cohorts combined, there were statistically significant decreases from baseline in IOP in both treatment groups and the decrease were similar in the dorzolamide and timolol groups with mean change changes from baseline (95% CI) in IOP of -7.20 (-8.53, -5.79) vs. -7.60 (-9.45, -5.75) mm Hg. The difference between the two treatments and the 95% CI for the difference were 0.44 (-1.92, 2.79) mm Hg, indicating a similar effect for the two treatment groups.

5.2 Conclusions and Recommendations

The data from this pediatric study for marketing exclusivity extension demonstrated that dorzolamide ophthalmic solution resulted in significant reduction of intraocular pressure (IOP) 'after treatment' compared with 'before treatment' in pediatric patients with glaucoma of age less than 6. Also, it appears that the proportion of discontinuation of therapy due to a drug-related adverse experience was within prespecified limits.

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