20 February 2013
EMA/109348/2013
Committee for Medicinal Products for Human Use (CHMP)

Aerius / Azomyr / Neoclarityn

(desloratadine)

Procedure Nos: EMEA/H/C/000313/A46/0060
EMEA/H/C/000310/A46/0060
EMEA/H/C/000314/A46/0060

CHMP assessment report for paediatric use studies submitted according to Article 46 of the Regulation (EC) No 1901/2006

Assessment Report as adopted by the CHMP with all information of a commercially confidential nature deleted

Disclaimer: The assessment report was drafted before the launch of the European Medicines Agency's new corporate identity in December 2009. This report therefore has a different appearance to documents currently produced by the Agency.

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ADMINISTRATIVE INFORMATION

Currently approved indication(s):	Aerius is indicated for the relief of symptoms associated with: - allergic rhinitis - urticaria
Pharmaceutical form(s) affected by this variation:	Film-coated tablet, Syrop, Oral Lyophilisate
Strength(s) affected by this variation:	All strengths
Rapporteur :	Pieter Neels
Timetable:	
Start	20/09/09
Date of this report	30/10/09
CHMP adoption	19/11/09

I. INTRODUCTION

Schering-Plough submits, in accordance with Article 46 of Regulation (EC) N°1901/2006, to the EMEA final reports for below listed studies.

P04683 Double-Blind, Randomized, Placebo-Controlled, Parallel-group, Multicenter/Multinational, Efficacy and Safety Study of Desloratadine (SCH 34117) 5 mg in the Treatment of Subjects with Allergic Rhinitis who Meet the Criteria for Intermittent Allergic Rhinitis (IAR);

P04684 Double-Blind, Randomized, Placebo-Controlled Parallel-group, Multicenter/Multinational, Efficacy and Safety Study of Desloratadine (SCH 34117) 5 mg in the Treatment of Subjects with Allergic Rhinitis who meet the Criteria for Persistent Allergic Rhinitis (PER);

P04446 Non-Interventional Trial of the Safe Use of Aerius (Desloratadine SCH 34117) in Paediatric Patients with Allergic Rhinitis or Chronic Idiopathic Urticaria;

P04706 Post-Marketing Surveillance Study of the Safety, Tolerability and Efficacy of Desloratadine Tablet among Filipino Patients.

A short critical expert overview has also been provided.

Schering- Plough Europe states that all above listed studies are stand alone studies. Schering- Plough Europe states that, in accordance with Article 16(2) of Regulation (EC) Nc 72612004, the data submitted do not influence the benefit-risk balance for Azomyr, Aerius and Neoclarityn and therefore do not require to take further regulatory action on the marketing authorisations for Azomyr, Aerius and Neoclarityn.

II. PRODUCT DEVELOPMENT RATIONALE

The purpose of this file is to summarize pediatric data with desloratadine collected by the Market Authorisation Holder in four studies with pediatric and/or adolescent subjects that have not been previously submitted to the EMEA.

Desloratadine (DL) is a second-generation, non sedating, oral, selective, peripheral H1-receptor antagonist that is approved and marketed in the European Union for the treatment of allergic rhinitis and urticaria. DL Tablets were first approved in January 2001 for use in adolescent and adult patients 12 years of age and older. DL syrup was initially approved in April 2002 for pediatric use down to 2 years of age, and extended in September 2004 for use down to 1 years of age.

The once-daily 5-mg DL tablet, RediTabs (orodispersible) tablet, and DL syrup (10 mL) are approved in adults and adolescents 12 years of age and over. The once-daily DL 2.5-mg RediTabs (orodispersible) tablet and DL syrup (5 mL) are approved in children 6 to 11 years of age. The DL syrup (2.5 mL) is approved in children 12 months to 5 years of age at a dose of 1.25 mg once daily. In the EU, a sugar-and dye-free DL oral solution has replaced the syrup at the same dosages. Desloratadine is indicated in the EU for the

relief of the symptoms of allergic rhinitis (including intermittent and persistent allergic rhinitis) and urticaria in patients down to 1 year of age.

The four studies described in this file included a total of 4374 subjects. Two studies (Study Nos. P04446 and P04706) included 133 pediatric subjects between 1 and 11 years of age and three studies (Study Nos. P04683, P04684, and P04706) included 244 adolescent subjects between 12 and 17 years of age and 3994 subjects ≥18 years of age. The ages of three subjects in Study No. P04706 were not specified. A list of studies included in this response is presented in Table 2.

III. SUBMITTED DATA

Table 2 Summary of Studies

Protocol No.	Study Description	Study Design	Study Population (Actual number, age range [yr], race, gender)	Study Population (Number of subjects by age group [by treatment group])[a]
P04446	Efficacy and Safety	Non-interventional, multicenter. 1.25 mg DL syrup (2.5 mL)	100; 1-5; 100C; 45F, 55M	Children: 100 (DL: 100) Adolescents: 0 Adults: 0
P04683	Efficacy and Safety	Double-blind, randomized, placebo-controlled, parallel-group, multicenter/multinational. 5 mg, DL tablets Placebo tablets	547; 13-72; 497C, 50NC; 318F, 229M	Children: 0 Adolescents: 20 (DL: 12; Placebo: 8) Adults: 527 (DL: 264; Placebo: 263)
P04684	Efficacy and Safety	Double-blind, randomized, placebo-controlled, parallel-group, multicenter/multinational. 5 mg, DL tablets Placebo tablets	716; 13-82; 655C, 61NC; 406F, 310M	Children: 0 Adolescents: 18 (DL: 9; Placebo: 9) Adults: 698 (DL: 351; Placebo: 347)
P04706	Efficacy and Safety	Open-label, post-marketing surveillance study. 5 mg, DL tablets 2.5 mg, DL syrup	3011; 3-91; 3011A; 1789F, 1222M	Children: 33 Adolescents: 206 Adults: 2769 Not specified: 3

Abbreviations: DL – desloratadine; yr – years; Race: A – Asian: C – Caucasian, NC – non-Caucasian; Gender: F – female, M – male.

a: Children ages 1 to 11 years; adolescents ages 12 to 17 years; adults ≥18 years.

Study P04683

Double-Blind, Randomized, Placebo-Controlled, Parallel-Group, Multicenter/Multinational, Efficacy and Safety Study of Desloratadine 5 mg in the Treatment of Subjects With Allergic Rhinitis Who Meet the Criteria for Intermittent Allergic Rhinitis (IAR) (SCH 34117).

Objective(s):

Primary: The primary objective was to compare the efficacy and safety of desloratadine (DL) with placebo in the symptomatic treatment of subjects 12 years and older with intermittent allergic rhinitis (IAR).

Secondary: The secondary objectives were to compare the effects of DL to those of placebo on quality of life and impact on productivity and health care utilization.

Number of subjects: 547.

Diagnosis and Criteria for Inclusion: Subjects 12 years of age or older, of either sex with at least a 2-year history consistent with allergic rhinitis who met the criteria for IAR (defined as symptoms of allergic rhinitis present less than four days per week or for less than four consecutive weeks per year) were to be included in the study.

Duration of Treatment: 15 days.

Results

Efficacy

Primary endpoint: The primary efficacy analysis was performed on the change from baseline in the subjects AM/PM PRIOR total 5 symptom score (T5SS) over Days 1 to 15 of treatment. T5SS = Severity scores for five individual allergic rhinitis symptoms (nasal congestion/stuffiness, sneezing, rhinorrhea/nasal discharge, nasal pruritus and ocular pruritus). Each symptom was scored 0 to 3. The scores were defined for T5SS as 0: no symptoms to 15: all severe symptoms. Analyses were performed using an analysis of variance (ANOVA), extracting sources of variation due to treatment and site.

A significantly greater decrease from baseline in the average AM/PM-PRIOR T5SS over days 1 to 15 was seen with DL vs. Placebo (-3.01 vs. -2.13; P<0.001). Significantly greater decreases in AM/PM-PRIOR T5SS with DL vs. Placebo occurred from Day 1 (P= 0.001) and on all 15 days of the study (P≤0.013). The significant effect of DL on T5SS endured across the full 24-hour dosing period (AM NOW T5SS) as early as the first full 24-hour measurement on Day 2 (P< 0.001) and averaged over Days 2 to 15 (P< 0.001).

Key Secondary Endpoint: The key secondary endpoint was the change from baseline in the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ-S) Total Score at the Final Visit (Endpoint evaluation as LOCF to the Final Visit). The RQLQ-S was only completed for subjects ≥18 years of age. The RQLQ Total Score was analyzed using the same ANOVA as specified for the primary endpoint. A significantly greater decrease (improvement) from baseline in total RQLQ-S score was seen in the DL group (-1.10 [-38.2%]) vs placebo (-0.73 [-24.9%]) (P< 0.001) at the study endpoint. Since statistical significance of the primary efficacy variable was achieved, the overall alpha level of 5% is preserved for total RQLQ-S.

The RQLQ-S domains of activity, non-nose/eye symptoms, practical problems, nasal symptoms, eye symptoms and emotion scores were also significantly improved with DL vs placebo (P≤0.007). Subjects with severe symptom score (with higher baseline diary T5SS [≥8.5/15]) had larger improvements from baseline in total RQLQ-S with DL vs placebo, with an effect size (0.55).

Secondary endpoints: In addition to the AM/PM PRIOR T5SS, a significantly greater improvement from baseline in average AM/PM PRIOR nasal congestion scores over days 1 to 15 was seen with DL vs. Placebo (-0.56 vs. -0.43, respectively; P=0.013). This benefit favoring DL was seen as early as Day 1 of treatment (p<0.017). Nasal congestion was significantly lower with DL vs. Placebo at the end of the first 24-hour dosing interval (AM NOW Day 2; P≤0.001). Mean AM/PM PRIOR scores for rhinorrhea, sneezing and nasal itching were also significantly lower in the DL vs. Placebo on Day 1, over week 1, week 2 and over Days 1 to 15 (P≤0.033). Eye itching was significantly lower in the DL group over week 1 (P=0.021) and was numerically lower over Days 1 to 15 (P= 0.051). Rhinorrhea, sneezing, eye itching and nasal itching scores at the end of the 24-hour dosing period (AM NOW) were significantly lower with DL at Day 2 (end of the first 24- hour interval; (P≤0.035)) and across Days 2 to 15 (P≤0.036).

A significantly greater decrease (improvement) from baseline in total RQLQ score was seen in the DL group (-1.10 [-38.2%]) versus Placebo (-0.73 [-24.9%]) (P<0.001) at the study endpoint. The RQLQ domains of activity, non-nose/eye symptoms, practical

problems, nasal symptoms, eye symptoms and emotion scores were also significantly improved with DL versus Placebo (P≤0.007). Subjects with severe symptom score at baseline (higher baseline diary T5SS [≥8.5/15]) had larger improvements from baseline in total RQLQ with DL versus Placebo, with an effect size (0.55).

The evaluation of therapeutic response by subjects in the DL 5- mg treatment group at the final visit (LOCF to the Final Visit) (3.24) was significantly lower (improved) than the evaluation of subjects in the placebo group (3.66) (P< 0.001).

There was a significantly greater decrease from baseline in the VAS score with DL (-17.2 [-30.6%]) versus Placebo (-10.9 [-17.0%]) (P< 0.001). The VAS score was significantly improved with DL on all treatment days.

The DL group had greater improvements from baseline in scores for interference with sleep than placebo over the duration of the study (P= 0.039). The DL group had greater improvements from baseline in scores for interference with activities of daily living than placebo over the duration of the study (P< 0.001).

Safety
There were relatively few adverse events reported by the subjects in this study. The overall incidence of treatment-emergent adverse events was comparable between the DL 5-mg group (20.7%) and the Placebo group (21.0%). Additionally, neither treatment group had a greater frequency of any adverse event relative to the other treatment group. The only adverse event that was reported by more than 5% of subjects was headache, which was reported by 18 subjects (6.5%) in the DL 5- mg group and 17 subjects (6.3%) in the placebo group. No pattern of adverse events occurred at a greater frequency in the DL 5-mg group compared to the placebo group. The number of subjects who experienced treatment-related adverse events was similar between the DL 5-mg treatment group (20 subjects [7.2%]) and the placebo group (19 subjects [7.0%]). The most frequently occurring treatment-related adverse event was headache, which was reported by 7 subjects (2.5%) in the DL 5- mg group and by 5 subjects (1.8%) in the placebo group. All other treatment- emergent adverse events occurred in <2% of subjects in either treatment group. There were no deaths or severe or life-threatening adverse events in this study.

Table 11 Incidence of Treatment-Emergent Adverse Events Reported by ≥1% of by Body System/Organ Class (All Randomized Subjects)

Protocol No. P04683

Body System Organ Class	Number (%) of Subjects			
	12 to 17 Years Old		≥18 Years Old	
	DL 5 mg (n=12)	Placebo (n=8)	DL 5 mg (n=264)	Placebo (n=263)
Subjects Reporting any Adverse Event	2 (16.7)	2 (25.0)	55 (20.8)	56 (21.3)
Gastrointestinal Disorders				
Dry Mouth	0	0	3 (1.1)	0
Nausea	0	0	4 (1.5)	3 (1.1)
Vomiting	0	0	3 (1.1)	0
General Disorders and Administration Site Conditions				
Fatigue	0	0	5 (1.9)	2 (0.8)
Thirst	0	0	1 (0.4)	4 (1.5)
Infections and Infestations				
Nasopharyngitis	1 (8.3)	0	4 (1.5)	6 (2.3)
Musculoskeletal and Connective Tissue Disorders				
Back Pain	0	0	3 (1.1)	2 (0.8)
Nervous System Disorders				
Headache	1 (8.3)	2 (25.0)	17 (6.4)	15 (5.7)
Somnolence	0	0	5 (1.9)	1 (0.4)
Respiratory, thoracic, and Mediastinal Disorders				
Cough	0	0	3 (1.1)	2 (0.8)
Dyspnoea	0	0	0	3 (1.1)
Pharyngolaryngeal Pain	0	0	3 (1.1)	5 (1.9)

DL – desloratadine.

Study P04684

Double-Blind, Randomized, Placebo-Controlled, Parallel-group, Multicenter/Multinational, Efficacy and Safety Study of Desloratadine (SCH 34117) 5 mg in the Treatment of Subjects With Allergic Rhinitis Who Meet the Criteria for Persistent Allergic Rhinitis (PER)

Objective(s):

Primary Objective: The primary objective was to compare the efficacy and safety of desloratadine (DL) with placebo in the symptomatic treatment of subjects 12 years and older with persistent allergic rhinitis (PER).

Secondary Objectives: The secondary objectives were to compare the effects of DL to those of placebo on quality of life and impact on productivity and health care utilization.

Number of subjects: 716.

Diagnosis and Criteria for Inclusion: Subjects 12 years and older, of either sex with at least a 2-year history of allergic rhinitis who met the criteria for PER (defined as symptoms of allergic rhinitis that were present for four days or more per week and for four or more consecutive weeks per year) were selected for the study.

Duration of Treatment: 12 weeks.

Results

Efficacy

Primary efficacy Variable:

The primary efficacy analysis was performed on the change from baseline in the subjects' AM/PM PRIOR T5SS over days 1 to 29 of treatment. T5SS = Severity scores for five individual allergic rhinitis symptoms (nasal congestion/stuffiness, sneezing, rhinorrhea/nasal discharge, nasal pruritus and ocular pruritus). Each symptom was scored 0 to 3. The scores were defined as 0: no symptoms to 15: all severe symptoms. Analyses were performed using an analysis of variance (ANOVA), extracting sources of variation due to treatment and site.

A significantly greater decrease form baseline in the average AM/PM-PRIOR T5SS over days 1 to 29 was seen with DL vs placebo (-3.76 vs -2.87; $p<0.001$). Significantly greater decreases were observed from day 1 with DL vs Placebo in AM/PM-PRIOR T5SS ($p=0.010$) and with all individual symptom scores ($p\leq0.006$) on Days 1 to 29.

In addition to the T5SS, a significantly greater improvement from baseline in average AM/PM PRIOR nasal congestion scores over Days 1 to 29 was seen with DL vs Placebo (- 0.69 vs. - 0.53, respectively; $P=0.002$). Mean AM/PM PRIOR scores for rhinorrhea and eye itching were significantly lower with DL vs Placebo as early as Day 1 ($P\leq0.042$), score for sneezing was significantly lower with DL vs Placebo as early as Day 2 ($P\leq0.016$), and nasal itching were significantly lower with DL vs Placebo on Day 3 ($P= 0.005$).

Safety

There were relatively few adverse events reported by the subjects in this study. The overall incidence of treatment-emergent adverse events was comparable between the DL 5 mg group (40.6%) and the placebo group (34.6%). The DL 5 mg group had a somewhat greater incidence of nasopharyngitis (10.6% vs 4.8%), somnolence (2.2% vs 0.3%), and cough (2.8% vs 1.4%). Subjects in the placebo group had a somewhat greater incidence of headache (10.4%) compared to the DL 5 mg group (6.9%). The only adverse events that were reported by more than 5% of subjects were headache, which was reported by 25 subjects (6.9%) in the DL 5 mg group and 37 subjects (10.4%) in the placebo group, and nasopharyngitis, which was reported by 38 subjects (10.6%) of subjects in the DL 5 mg group and by 17 subjects (4.8%) of subjects in the placebo group. The number of subjects who experienced treatment-related adverse events was similar between the DL 5 mg treatment group (36 subjects [10.0%]) and the placebo group (30 subjects [8.4%]). The two most frequently occurring treatment-related adverse events were fatigue, which was reported by 7 subjects (1.9%) in the DL 5 mg group and by 9 subjects (2.5%) in the placebo group and headache, which was reported by 6 subjects (1.7%) in the DL 5 mg group and by 7 subjects (2.0%) in the placebo group. All other treatment-related treatment-emergent adverse events occurred in < 2% of subjects in either treatment group.

The number of severe adverse events was similar between the two treatment groups. Most severe adverse events were only reported by one subject each. The most commonly reported severe adverse events were headache, which was reported by 3 subjects (0.8%) in the DL 5 mg group and by 5 subjects (1.4%) in the placebo group. In

addition two subjects (0.6%) in the placebo group also reported sinus headaches and one subject (0.3%) in the placebo group reported migraine that were considered severe by the investigator. Sinus headache and migraine were not reported by subjects in the DL 5 mg group. Fatigue and gastroenteritis were reported by three subjects (0.8%) and two subjects (0.6%), respectively in the DL 5 mg group. These two adverse events were not reported by subjects in the placebo group. All other severe adverse events were reported by one subject each.

There was one life-threatening adverse event reported by a subject in the placebo group. Subject No. 1449 experienced a myocardial infarction that was considered unrelated to study treatment. The subject was discontinued from the study.

There were five severe adverse events (0.7%) that were considered by the investigator to be either possibly or probably related to study treatment. Three severe adverse events (0.7%) were reported by subjects in the DL 5 mg group and two severe adverse events (0.5%) were reported by subjects in the placebo group.

There were three subjects (0.4%) who experienced four serious adverse events reported during the study. None of the serious adverse events were considered related to study treatment. One subject (Subject No. 1453) in the DL 5- mg group reported a serious adverse event (lower limb fracture). Two subjects in the placebo group reported serious adverse events. Subject No. 756 experienced a diverticulum intestinal and Subject No. 1449 experienced a bronchospasm and acute myocardial infarction, which was considered life threatening by the investigator. One subject (Subject No. S00006) who was screened but was not randomized to study drug experienced dizziness, ataxia, nausea, vomiting, spondylosis arterial hypertension, and a transient ischemic attack. The transient ischemic attach was considered life-threatening.

A total of 23 subjects (3.2%) were discontinued from the study because of adverse events: seven subjects (1.9%) in the DL 5-mg treatment group and 16 subjects (4.5%) in the placebo group. One subject (Subject No. 001453) in the DL 5-mg treatment group and two subjects (Subject Nos. 000756 and 001449) in the placebo group had adverse events that were considered severe, but these adverse events were considered unlikely related to study treatment by the investigators. One of the adverse events (acute myocardial infarction) experienced by Subject No. 001449 was considered life threatening by the investigator. All other adverse events that resulted in discontinuation from the study, including adverse events that were considered to be possibly or probably related to study drug, were considered to be mild-to-moderate in severity.

Four subjects in the DL 5 mg group and two subjects in the placebo group had their treatment interrupted due to adverse events. All adverse event leading to study drug interruption were considered mild-to-moderate in severity and were considered unlikely related to study treatment.

Table 12 Incidence of Treatment-Emergent Adverse Events Reported by ≥1% of Subjects by Body System/Organ Class (All Randomized Subjects)

Protocol No. P04684

Body System Organ Class	Number (%) of Subjects			
	12 to 17 Years Old		≥18 Years Old	
	DL 5 mg (n=9)	Placebo (n=9)	DL 5 mg (n=351)	Placebo (n=347)
Subjects Reporting any Adverse Event	4 (44.4)	3 (33.3)	142 (40.5)	120 (34.6)
Ear and Labyrinth Disorders				
Ear Pain	0	0	4 (1.1)	0
Gastrointestinal Disorders				
Nausea	0	0	3 (0.9)	6 (1.7)
General Disorders and Administration Site Conditions				
Asthenia	0	0	4 (1.1)	3 (0.9)
Fatigue	0	0	13 (3.7)	11 (3.2)
Pyrexia	0	1 (11.1)	6 (1.7)	5 (1.4)
Infections and Infestations				
Gastroenteritis	0	0	4 (1.1)	1 (0.3)
Influenza	0	0	5 (1.4)	4 (1.2)
Nasopharyngitis	2 (22.2)	0	36 (10.3)	17 (4.9)
Upper Respiratory Tract Infection	0	0	5 (1.4)	3 (0.9)
Urinary Tract Infection	0	0	4 (1.1)	3 (0.9)
Musculoskeletal and Connective Tissue Disorders				
Back Pain	1 (11.1)	0	5 (1.4)	3 (0.9)
Myalgia	0	1 (11.1)	2 (0.6)	2 (0.6)
Neck Pain	1 (11.1)	0	1 (0.3)	2 (0.6)
Pain in Extremity	1 (11.1)	0	2 (0.6)	3 (0.9)
Nervous System Disorders				
Headache	1 (11.1)	1 (11.1)	24 (6.8)	36 (10.4)
Migraine	1 (11.1)	0	1 (0.3)	1 (0.3)
Sinus Headache	0	0	2 (0.6)	4 (1.2)
Somnolence	0	0	8 (2.3)	1 (0.3)
Respiratory, Thoracic, and Mediastinal Disorders				
Asthma	0	0	3 (0.9)	4 (1.2)
Cough	1 (11.1)	0	9 (2.6)	5 (1.4)
Epistaxis	0	0	5 (1.4)	2 (0.6)
Pharyngolaryngeal Pain	0	0	12 (3.4)	9 (2.6)
Skin and Subcutaneous Tissue Disorders				
Angioedema	0	1 (11.1)	0	0
Pruritus	0	0	4 (1.1)	6 (1.7)

Abbreviation: DL - desloratadine

Study P04446

Non-Interventional Trial of the Safe Use of Aerius (Desloratadine) in Pediatric Patients With Allergic Rhinitis or Chronic Idiopathic Urticaria.

Objective(s):

The objective of this non-interventional study was to evaluate the safety of Aerius syrup in pediatric patients aged 1 to 5 years old with allergic rhinitis or chronic idiopathic urticaria.

Number of subjects: 100.

Diagnosis and Criteria for Inclusion: Pediatric patients aged 1 to 5 years old with allergic rhinitis or chronic idiopathic urticaria.

Duration of treatment: 1 to 9 weeks.

Results

Efficacy

Efficacy of the DL 1.25 mg dose of Aerius syrup was evaluated and measured by the amount of relief each subject experienced from the baseline visit to the final visit. Eighty-eight subjects (88.9%) reported either marked or complete relief. Only two subjects (one subject with each condition) reported treatment failure.

Most subjects (77 subjects) showed an improvement in symptoms from Baseline to Follow-up. None of the subjects showed a worsening of symptoms from Baseline to Follow-up, and only 22 subjects reported that their symptoms remained the same. Most subjects (20 subjects [20%]) who reported no change in symptoms evaluated their symptoms as “mild” at Baseline, and two subjects (2.0%) evaluated their symptoms as “moderate” at Baseline. There were four subjects whose symptoms were “severe” at Baseline. The symptoms of two of these subjects were improved to “moderate” and the symptoms of two of these subjects were improved to “mild”.

Safety

Forty-five of the 100 subjects (45.0%) reported adverse events in this study. Only four adverse events were reported by at least 5% of subjects. Vomiting and cough were reported by 6 subjects (6.0%) each and diarrhoea and bronchitis were reported by 5 subjects (5.0%) each.

Ten subjects (10.0%) reported treatment-emergent adverse events that were considered possibly related to treatment with desloratadine. The most common treatment-related, treatment-emergent adverse event was diarrhoea, which occurred in 4 subjects. Most of these adverse events were considered mild-to-moderate in severity. Subject 10/04 experienced emotional distress that was considered severe and possibly related to treatment. This subject discontinued treatment due to this adverse event. No other treatment-related adverse event was considered severe.

There were no life-threatening adverse events in this study. Two subjects experienced adverse events that were considered severe. Subject 10/04 experienced emotional distress that was considered severe and possibly related to treatment. This subject discontinued treatment due to this adverse event. Subject 03/08 experienced pyrexia, tonsillitis, and vomiting that were considered severe. The subject also experienced dehydration, which was considered moderate in severity, and resulted in interruption of treatment. These were serious adverse events that were considered unlikely related to treatment.

Table 10 Summary of Treatment-Emergent Adverse Events Reported by ≥2% of Subjects by System Organ Class

Protocol No. P04446

	Number (%) of Subjects
	DL 1.25 mg (n=100)
System Organ Class	
Subjects Reporting any Adverse Event	**45 (45)**
Gastrointestinal Disorders	
Abdominal Pain	3 (3)
Diarrhoea	5 (5)
Dyspepsia	3 (3)
Vomiting	6 (6)
General Disorders and Administration Site Conditions	
Pyrexia	4 (4)
Infections and Infestations	
Bronchitis	5 (5)
Nasopharyngitis	4 (4)
Pharyngitis	4 (4)
Rhinitis	2 (2)
Tonsillitis	3 (3)
Respiratory, Thoracic, and Mediastinal Disorders	
Cough	6 (6)
Skin and Subcutaneous Tissue Disorders	
Urticaria	2 (2)

DL – desloratadine.

Study P04706

Post-Marketing Surveillance Study of the Safety, Tolerability and Efficacy of Desloratadine Tablet among Filipino Patients.

Objectives(s): Primary objective is to evaluate the overall safety and tolerability of Desloratadine Tablet when used in patients with either Allergic Rhinitis or Chronic Idiopathic Urticaria. Secondary objective is to evaluate the efficacy of Desloratadine Tablet in relieving the symptoms of patients with either Allergic Rhinitis or Chronic Idiopathic Urticaria.

Number of subjects: There were a total of 3085 patients enrolled in the study. The sex distribution was 40.66% of the patient were male while 59.34% were female. The average age of the patient was 35.84 with the oldest patient at 91.

Diagnosis and Criteria for Inclusion: Adult patients who were diagnosed with Allergic Rhinitis or Chronic Idiopathic Urticaria.

Duration of Treatment: Desloratadine Tablets were taken for 14 days and were asked to follow up on the 15th day where safety, tolerability and efficacy variables were measured.

Results

Safety and Tolerability

A total of 57 patients (1.88%) reported to have experienced an adverse drug event (ADE). All of these patients have experienced only one event. The most common

adverse event was dizziness/drowsiness (31.58%), followed by sedation (21.05%). A total of 30 AEs (54.55%) of the reported AEs were indicated as treatment-related. In terms of the patients' global assessment of tolerability of the study drug, a total of 1184 patients (41.20%) gave a rating of Excellent, 1288 (44.82%) gave a rating of Very Good, 364 patients (12.67%) gave a rating of Good, 32 patients (1.11%) gave a rating of Fair and 6 patients (0.21%) gave a rating of poor.

Table 13 Summary of Adverse Events

Protocol No. P04706

	<12 Years Old (n=33)	12 to 17 Years Old (n=206)	≥18 Years Old (n=2769)	Total (n=3011)
Subjects Reporting any Adverse Event	**1**	**2**	**54**	**57**
Abdominal Pain	0	0	1	1
Dizziness	0	0	1	1
Drowsiness	1	1	14	16
Dryness of Mouth	0	0	2	2
Dryness of Mucous Membrane	0	0	1	1
Dryness of Throat	0	0	3	3
Episodes of Diarrhea	0	1	0	1
GI Irritation	0	0	3	3
Headache	0	0	6	6
Inability to Sleep	0	0	1	1
Nausea	0	0	2	2
Palpitations	0	0	1	1
Productive Cough	0	0	1	1
Rashes	0	0	1	1
Sedation	0	0	12	12
Slight Drowsiness	0	0	1	1
Somnolence	0	0	1	1
Vomiting	0	0	2	2
Weakness	0	0	1	1

Efficacy

34.87% of the patients who completed the study achieved clinical cure. 63.45% of the patients who completed the study experienced an improvement from their initial condition. 1.37% reported no improvement from their initial condition.

Assessor's comment

The MAH only a submitted a synopsis of this clinical study. The Clinical Study Report is missing. The Applicant is asked to submit the entire Clinical Study Report.

IV. CONCLUSION AND RECOMMENDATION

The MAH submits the Clinical Study Reports for Study P04683, P04684, P04446 in accordance with Article 46 of regulation (EC) N°1901/2006. For Study P04706 only a synopsis is submitted. The MAH is asked to submit the full Clinical Study Report (Question 1).

The data in pediatric and adolescent patients are extended by these clinical studies.

The efficacy and safety results of these clinical studies are as expected. The incidence and types of adverse events reported in children and adolescents in these studies were similar to those seen in previously reported studies with DL in pediatric/adolescent

subjects and are indicative of common pediatric illnesses and the conditions that the subjects were being treated for in the studies.

The Rapporteur agrees with the MAH that these Clinical Studies do not change the efficacy or safety profile of desloratadine and no changes are deemed necessary to the prescribing information for desloratadine based on these clinical studies.

V. REQUEST FOR SUPPLEMENTORY INFORMATION

1. The MAH submits the Clinical Study Reports for Study P04683, P04684, P04446 in accordance with Article 46 of regulation (EC) N°1901/2006. For Study P04706 only a synopsis is submitted. The MAH is asked to submit the full Clinical Study Report