EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Medicinal Products for Human Use (CHMP)

Aerius, Azomyr, Neoclarityn

(desloratadine)

Procedure No: EMEA/H/C/000313-310-314/A46/0063

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

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1. Introduction

This report covers the following post-authorisation commitments undertaken by the MAH:

It concerns a submission according to the P-46 article of the EU Paediatric Regulation (EC No 1901/2006) i.e. the results of a clinical study (PN200) in perennial allergic rhinitis conducted in Japan with desloratadine in which 82 of the 608 randomized subjects were 12-17 years of age.

This study is not being submitted in support of a new pediatric indication for DL in the EU.

1.1. Steps taken for the assessment

Start of procedure:	24/04/2014
CHMP Rapporteur's preliminary assessment report circulated on:	23/09/2014
CHMP Rapporteur's updated assessment report circulated on:	13/10/2014

2. Assessment of the post-authorisation measure

PN200
Study design: double-blind, randomized, placebo-controlled clinical trial to study the safety and efficacy of desloratadine (DL) 5-mg tablets in Japanese subjects 12 years and older with perennial allergic rhinitis.

Participants: 608 randomized subjects including 82 subjects that were 12-17 years of age.

Study medication: during the screening period, the subjects took placebo (in a single-blind run-in period) for 7 days. After the screening period, subjects meeting all eligibility criteria received study treatment orally for 2 weeks in a double-blinded manner. They were randomized to one of 3 treatments:

- DL 10 mg once daily (10 mg group)
- DL 5 mg once daily (5 mg group)
- Placebo once daily (placebo group)

Primary efficacy endpoint: change from baseline in the total nasal symptom score (TNSS), the total of the four nasal symptom scores (sneezing, rhinorrhea, nasal congestion, and nasal itching), as assessed by the (sub-) investigator at Week 2.

Efficacy Results: Primary endpoint:

Treatment	N	Baseline Mean(SD)	Week 2 Mean(SD)	TNSS Change from Baseline at Week 2	
				Mean(SD)	LS Mean(95% CI)†
DL 10 mg	203	7.34(1.90)	5.36(2.09)	-1.99(2.21)	-1.94(-2.23,-1.65)
DL 5 mg	202	7.32(1.78)	5.30(2.26)	-2.01(2.32)	-1.96(-2.25,-1.67)
Placebo	201	7.19(1.85)	5.38(2.27)	-1.82(2.34)	-1.87(-2.16,-1.58)
Estimated Difference				Difference in LS Means(95% CI)	p-value
DL 10 mg vs. Placebo				-0.08(-0.48,0.32)	0.707
DL 5 mg vs. Placebo				-0.09(-0.49,0.31)	0.661

†Based on cLDA model with terms of visit, visit-by-treatment, visit-by-age strata, visit-by-severity interactions; visit is treated as a categorical variable.
N = Number of subjects with baseline or at least one post baseline observation.
TNSS = Total nasal symptom score, the sum of the four nasal symptom scores of nasal congestion, rhinorrhea, nasal itching and sneezing.
CI = Confidence Interval; LS Mean = Least-Squares Mean; SD = Standard Deviation.
DL: Desloratadine

Conclusion on efficacy:

The change from baseline in the primary endpoint TNSS was comparable between DL 10 mg group or 5 mg group and placebo group, and ***no superiority to placebo group was shown for the DL 10 mg and 5 mg groups***.

Safety Results

Treatment period starts from the first dose day of study medication until 14 follow-up days after the last dose day of study medication.

	DL 5 mg		DL 10 mg		Placebo	
	n	(%)	n	(%)	n	(%)
Subjects in population	202		203		201	
with one or more adverse events	27	(13.4)	29	(14.3)	20	(10.0)
with no adverse event	175	(86.6)	174	(85.7)	181	(90.0)
with drug-related† adverse events	0	(0.0)	6	(3.0)	2	(1.0)
with serious adverse events	1	(0.5)	0	(0.0)	0	(0.0)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)	0	(0.0)
discontinued‡ due to an adverse event	1	(0.5)	0	(0.0)	2	(1.0)
discontinued due to a drug-related adverse event	0	(0.0)	0	(0.0)	1	(0.5)
discontinued due to a serious adverse event	1	(0.5)	0	(0.0)	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)

† Determined by the investigator to be related to the drug.
‡ Study medication withdrawn.
DL: Desloratadine
Treatment period starts from the first dose day of study medication until 14 follow-up days after the last dose day of study medication.

The incidence of adverse events was 13.4% (27/202 subjects) for DL 5 mg group, 14.3% (29/203 subjects) for DL 10 mg group and 10.0% (20/201 subjects) for placebo group.

The incidence of drug-related adverse events was 0.0% (0/202 subject) for DL 5 mg group, 3.0% (6/203 subjects) for DL 10 mg group and 1.0% (2/201 subjects) for placebo group suggesting that the **incidence was similar among all treatment groups**.

No deaths were reported.

One serious adverse event of severe epilepsy was reported in the DL 5 mg group and was not considered by the investigator to be related to the study drug.

The incidence of **treatment discontinuation due to adverse events** was 0.5% (1/202 subject) for the DL 5 mg group, 0.0% (0/203 subject) for DL 10 mg group and 1.0% (2/201 subjects) for placebo group. The adverse events resulting in treatment discontinuation included epilepsy (1 subject in the DL 5 mg group), nasopharyngitis (1 subject in the placebo group) and urticaria (1 subject in the placebo group). All of these adverse events were resolved after discontinuation of treatment.

Conclusion on safety:

The safety profile of DL 10 mg and 5 mg administered once daily for 14 days was ***comparable*** to placebo; they were well-tolerated.

Assessment of the necessity for an update of the EU SmPC:

The SmPC already contains the following information in this context:

- 4.2 “There is ***limited*** clinical trial efficacy experience with the use of desloratadine in adolescents 12 through 17 years of age”.
- 5.1 “The efficacy of Aerius/Azomyr/Neoclarityn ***has not been clearly demonstrated*** in trials with adolescent patients 12 through 17 years of age.”

The results of the study are covered by what is already mentioned in the SmPC about the efficacy of desloratadine in adolescent patients. Therefore, it is concluded that no update to the EU is necessary.

PAM fulfilled (all commitments fulfilled) - No further action required