EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Procedure Management and Committees Support Division

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

Xolair

omalizumab

Procedure no: EMEA/H/C/000606/P46/045

Note

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

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Final Rapporteur's Assessment Report for the Post-Authorisation Measure EMEA/H/C/606 P46 045

Xolair

International non-proprietary name: omalizumab

Procedure No. EMEA/H/C/606 P46 045

Marketing authorisation holder: Novartis Europharm Ltd, United Kingdom

Date of this report:	22 October 2015
Deadline for comments:	09 November 2015

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1. Introduction

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

On 14 Aug 2015 the MAH submitted a study CIGE025ACA07 including pediatric subjects for Xolair in accordance with Article 46 of Regulation (EC) No1901/2006, as amended, on medicinal products for paediatric use.

Study CIGE025ACA07 was a 12-month, open-label, single-arm study evaluating the oral corticosteroid (OCS) sparing effect of Xolair® (omalizumab) therapy in inadequately-controlled moderate to severe allergic asthma patients. This study was conducted in patients ≥12 years of age, in Canada. The study included one pediatric subject.

Xolair is approved as add-on therapy to children 6-12 years of age to improve asthma control in patients with severe persistent allergic asthma who have a positive skin test or in vitro reactivity to a perennial aeroallergen and frequent daytime symptoms or night-time awakenings and who have had multiple documented severe asthma exacerbations despite daily high-dose inhaled corticosteroids, plus a long-acting inhaled beta2-agonist. A similar indication is approved for adolescents and adults. It is also indicated for adults and adolescents (12 years of age and above) with chronic spontaneous urticaria (CSU) refractory to standard of care.

1.1. Steps taken for the assessment

Submission date:	14 August 2015
Start of procedure:	21 September 2015
CHMP Rapporteur's preliminary assessment report circulated on:	22 October 2015
CHMP Rapporteur's updated assessment report circulated on:	n/a
CHMP opinion:	19 November 2015

2. Assessment of the post-authorisation measure PAM P46 045

2.1. Purpose of submission

Study CIGE025ACA07 was a phase IV, 12-month, open-label, single-arm trial in patients ≥12 year of age with inadequately controlled moderate-severe allergic asthma which evaluated the oral corticosteroid (OCS) sparing effect of omalizumab when prescribed in routine clinical practice as per the Canadian Product Monograph (indication and dosing).

The primary objective of this study was to evaluate the OCS sparing effect of omalizumab in the study population by comparing OCS use during the 12-month, prospective study treatment period (Prospective period) with the historical documented use of OCS in the 12-month period prior to study enrolment (Retrospective period). The use of OCS was evaluated in terms of the mean change in total annual OCS dose during the prospective period as compared to the retrospective period.

One secondary objective was to evaluate the impact of omalizumab treatment on the rate of severe asthma exacerbations and symptom control.

A total of 99 subjects were enrolled in 25 sites, all located in Canada, and all subjects received at least one dose of omalizumab treatment. The mean age of patients enrolled in this study was 47.8 years, with age range of 12-77 years old. 68.7% of patients enrolled were females, and 87.9% were Caucasian.

The results of this study are now submitted to the CHMP according to Article 46 of Regulation (EC) No 1901/2006 since it includes one paediatric patient.

2.2. Efficacy results

The mean total annual dose of OCS use in the prospective period compared to the retrospective period (reduction by 1171.5 mg prednisone equivalents in the ITT population, $p<0.0001$).

The number of subjects experiencing at least one severe asthma exacerbation during the prospective period was less than half compared to the retrospective period (42 versus 92 subjects) and the mean number of severe asthma exacerbations reported during the prospective period was 0.8, compared with 2.4 during the retrospective period ($p<0.0001$).

CHMP comment: The primary endpoint of this study was reached as it was shown a corticosparing effect in the ITT population with omalizumab treatment with a reduction in oral cortisteroid annual dose in the prospective period compared to the retrospective period. As secondary endpoints it was shown a decrease in individuals experiencing asthma exacerbations and also a decrease in the total numbers of exacerbations in the population when comparing the prospective data to the retrospective.

2.3. Safety

In total, 9 subjects (9%) experienced 16 SAEs. The most common event of severe intensity was infections of infestations (n=5) including abscess, device related infection, post procedural infection, 1 event of each, and staphylococcal infection. Out of the 16 SAEs reported, 3 events were suspected to be related to omalizumab (2 anaphylactic reactions and 1 event of dizziness), all of which were experienced by the same subject.

2.4. Paediatric summary

There was one paediatric patient enrolled in study IGE025ACA07. Patient 0011-00008 was a 12 year old Caucasian male who was lost to follow up after visit 1 (screening/baseline visit). This patient received 1 omalizumab injection and was part of the safety population but not included in the ITT dataset. No AEs were reported for this patient.

CHMP comment: The MAH has presented paediatric data as requested in legislation. Only one paediatric patient was included in this study, why no conclusion can be drawn on efficacy in the paediatric population. In addition, only safety data is available for this paediatric patient. Safety was adequately documented and there were no unexpected findings.

3. CHMP overall conclusion

3.1. Overall conclusion

The presented data does not change the benefit risk for omalizumab in the paediatric approved indications. No changes are warranted in the SmPC.

3.2. Recommendation

No further action required.

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

☐ PAM not fulfilled (not all commitments fulfilled) and further action required: