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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/P46/044

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 044

Xolair

International non-proprietary name: omalizumab

Procedure No. EMEA/H/C/606 P46 044

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:

According to Article 46 of Regulation (EC) No 1901/2006 results of any marketing authorization holder sponsored study conducted in the paediatric population should be submitted to the competent authority. To comply with this requirement, Novartis presents data from Study IGE025AGB04, a multi-center, noninterventional, study of the impact of omalizumab on asthma control of patients with severe persistent allergic asthma for whom omalizumab was prescribed as part of usual clinical practice. The study was conducted in UK and enrolled 6 paediatric patients.

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.

1.1. Steps taken for the assessment

Submission date:	21 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 044

Study CIGE025AGB04 was an observational, prospective, study of the impact of omalizumab on asthma control and the lives of patients (≥16 years old) with severe persistent allergic asthma for whom omalizumab was prescribed as part of usual clinical practice. The study used a mixed methodology to obtain retrospective data on the 12 month period preinitiation of omalizumab, prospective or retrospective data for baseline (omalizumab initiation) data (depending on whether the patient was recruited to the study before or after omalizumab initiation), and prospective data at 16 weeks, 8 months and 12 months post-initiation of omalizumab. Enrolled patients had a diagnosis of severe persistent allergic asthma for whom a clinical decision to prescribe omalizumab had been made.

The purpose of this study was to measure the impact of omalizumab on patients' lives and the clinical management of severe asthma in the real world. The primary objective was to compare the mean daily dose of OCS prescribed per patient in the 12 months following initiation of omalizumab with the mean daily dose prescribed in the 12 months prior to omalizumab initiation.

A total of 258 patients took part in this study and 218 completed. Out of the 258 patients recruited, 168 (65.1%) were female and the mean age was 44.7 years (range from 16.5 years up to 79.7 years). The majority of patients enrolled were classified as White British.

Corticosteroid use

There was a significant reduction (-0.59 g; $p<0.001$) in the mean total dose of OCS prescribed per patient in the 12 months pre- compared to the 12 months post-initiation of omalizumab for the ITT group. The reduction in the mean daily dose of OCS for only those days where steroids were taken was -3.67 mg per day for the ITT group ($p<0.001$), -3.80 mg per day ($p<0.001$) for the responder subgroup and -1.42 mg ($p<0.05$) for the CCS subgroup. By 12 months 46.4% (98/211) of patients had stopped OCS in the ITT group, with 50% (90/180) of patients in the responder subgroup, and 15.8% (12/76) of patients stopping OCS in the CCS subgroup. The proportion of patients either stopping or reducing OCS by 12 months was 61.8%, 66.3% and 42.1% for the ITT, responder and CCSs groups, respectively.

Response rates

Overall, there were 197 (82.4%) patients classified as responders at 16 weeks, with a similar proportion (83.6%) of responders in the continuous corticosteroid (CCS) subgroup. For the intention-to-treat (ITT) population (n=235), the effectiveness of omalizumab was classified as either excellent or good in 66.8% of patients, using the Global Evaluation of Treatment Effectiveness (GETE) scale.

Exacerbations (hospital and assumed)

In the ITT group, the mean number of hospital exacerbations was reduced from 1.66 in the 12 months pre-omalizumab to 0.69 ($p<0.001$) in the 12 months post-omalizumab, which represents a 58.3% relative reduction. For the responder subgroup a relative reduction of 61.3% in hospital exacerbations was observed and for the CCS subgroup the reduction was 61.5%.
The mean number of assumed exacerbations (an exacerbation was assumed if a patient had an increase in OCS of 10 mg or more for at least 3 days) for the ITT group reduced by 44.7%, with a reduction of 48.9% in the responder subgroup, and a reduction of 34.2% in the CCS subgroup.

Paediatric population

Six (6) paediatric patients (≥16 and <18 years old) were enrolled in this trial. As paediatric patients in this study were not analysed separately, no specific information related to treatment efficacy is available from the CSR. Information regarding AEs in the paediatric patients enrolled was available through the study database. Two of these patients (both female) experienced AEs. A 16 year old patient experienced two AEs; one serious (vomiting-causality not suspected, patient had complete recovery) and one non-serious (maternal exposure during pregnancy-causality not assessable). The other patient was 17 years of age and suffered from the non-serious AE of drug ineffective, for which causality not assessable.

CHMP comment:

The company has presented paediatric data as requested in legislation. Only 6 paediatric patients were included in this study and efficacy data were not summarised. Thus no conclusion can be drawn on efficacy. Nevertheless, considering the low number of patients and their age (adolescents 16-18 years, thus a paediatric population for which no difference relatively adults would be expected) there is no need to further elaborate on efficacy in this population. Safety was adequately documented and there were no unexpected findings.

3. CHMP overall conclusion

Efficacy for the paediatric population was not summarised in this study and there were no specific safety concerns recorded. Benefit/risk remains positive for the paediatric population.

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