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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

Cervarix

HUMAN PAPILLOMAVIRUS VACCINE [TYPES 16, 18] (RECOMBINANT, ADJUVANTED, ADSORBED)

Procedure no: EMEA/H/C/000721/P46/085

Note

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

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Rapporteur's Assessment Report for the Post-Authorisation Measure

Cervarix

International non-proprietary name: HPV-16/18 VLP L1 AS04 vaccine

EMEA-H-C-721-FUM Article P46 085

Marketing authorisation holder:GSK

Date of this report:	19/03/2015
Deadline for comments:	08/04/2015

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1. Introduction

This report covers the following post-authorisation commitments undertaken by the MAH:
Extension study of the primary vaccination study, study HPV-013 and subsequent follow-up study Ext HPV-013 designed to evaluate the long-term immunogenicity and safety of the HPV-16/18 VLP L1 AS04 vaccine in pre-teen and adolescent females aged 10 to 14 years at the time of first vaccination, for a period of approximately 10 years after first HPV vaccination in the primary study (study HPV-013). *The current report presents the results of the interim analysis up to Month 108 (Year 9).*

1.1. Steps taken for the assessment

Submission date:	11/02/2015
Start of procedure:	22/02/2015
CHMP Rapporteur's preliminary assessment report circulated on:	24/03/2015
CHMP Comments	08/04/2015
CHMP opinion:	23/04/2015

2. Assessment of the post-authorisation measure PAM

This extension study of the primary vaccination study, study HPV-013 and subsequent follow-up study Ext HPV-013 was designed to evaluate the long-term immunogenicity and safety of the HPV-16/18 VLP L1 AS04 vaccine in pre-teen and adolescent females aged 10 to 14 years at the time of first vaccination, for a period of approximately 10 years after first HPV vaccination in the primary study (study HPV- 013). The current report presents the results of the interim analysis up to Month 108 (Year 9). No confirmatory analyses were performed on the primary or secondary objectives.

At Month 108, all subjects were still seropositive for both HPV-16 and HPV-18 antibodies. In the ATP cohort, in subjects who were initially seronegative, GMTs at Month 108 were 1949.2 EL.U/mL [95% CI: 1776.8 – 2138.5] for HPV-16 and 739.1 EL.U/mL [95% CI: 669.9 – 815.3] for HPV-18.

The HPV-16 and HPV-18 antibody titers in ATP baseline seronegative subjects were 4.66 and 3.05 fold higher, respectively, than the titers observed at an equivalent timepoint (i.e. Month 107 – Month 113 during the plateau phase) in female subjects aged 15-25 years at the time of enrolment in the HPV-001/007/023 study.

The HPV-16 and HPV-18 antibody titers in ATP baseline seronegative subjects were 65.41 and 32.56 fold higher, respectively, than those associated with natural infection found in subjects aged 15-25 years at the time of vaccination in study HPV-008.

During the follow-up period from Month 96 to Month 108, 15 subjects reported 22 SAEs, none of which were considered by the investigator to be causally related to vaccination. No fatal SAEs were reported during the follow-up period from Month 96 to Month 108.

In conclusion, the results from this interim analysis confirm the sustained immunogenicity of the HPV-16/18 L1 VLP AS04 vaccine up to 108 months after administration of the first dose in subjects aged 10 - 14 years at the time of first vaccination both in terms of anti-HPV-16/18 GMTs and seropositivity and with an acceptable safety profile.

The submission of the final analysis at month 120 to fulfill the commitment FUM.019 is currently planned by December 2015.

3. Rapporteur's overall conclusion

The MAH Discussion is generally endorsed. The results of this annual update report were in agreement with previous annual reports. The results are in line with expectations. The MAH's overall conclusions

are endorsed and no further actions are required for this PAM at Month 108. No further regulatory action is considered necessary based on these results. The final results of this study are expected at month 120. A complete safety profile of this long term follow up is expected at the end of the study including all subjects from the TVC that were originally selected for inclusion in HPV025 EXT-13.

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

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