EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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EMA/126295/2015
Committee for Medicinal Products for Human Use (CHMP)

CHMP assessment report for paediatric studies submitted in accordance with article 46 of regulation (EC) No1901/2006, as amended.

Prevenar 13

(Pneumococcal saccharide conjugated vaccine, adsorbed)

Procedure No. EMEA/H/C/001104

P46 044

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

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I. INTRODUCTION

On June 23, 2011 the MAH submitted a completed paediatric study for Prevenar 13, in accordance with Article 46 of Regulation (EC) No1901/2006, as amended, on medicinal products for paediatric use.

A short critical expert overview has also been provided.

The MAH stated that the submitted paediatric study does not influence the benefit risk for Prevenar 13 and that there is no consequential regulatory action.

This study was assessed in procedure EMEA/H/C/1104 P46 042. Two questions were raised in the final AR of that procedure, to which the MAH has no responded. The responses to these questions are assessed below.

II. SCIENTIFIC DISCUSSION

Clinical aspects
QUESTION 1
With regard to the pre-challenge serological data: From the supportive tables (Section 15, tables 12/15, 23/25, 41/43) it appears that OPA antibody titres and [geometric mean titers] GMTs are very similar between both groups on visit 1 (prior to vaccination), except for serotypes 6B, 18C and 23F. For the latter three the 7vPnC group consistently shows better protective values. The company is asked to comment on this and on the fact that there is no apparent difference in protection between groups with regard to the serotypes 4, 9V, 14 and 19F.

Response
In Study 3016, baseline serum levels of pneumococcal serotype-specific immunoglobulin G (IgG) and opsonophagocytic activity (OPA) were determined in children who had been vaccinated approximately 10 years previously with a 4-dose series of either 7vPnC or MnCC (doses at 2, 4, 6, and 12 to 15 months of age). At the time of enrollment in Study 3016, all subjects were between 11 and 14 years old. By this age, serum levels of anti-pneumococcal antibody are the result of a combination of infant vaccination as well as natural exposure, and it is not known whether vaccination in infancy is an important determinant of protection against pneumococcal disease among children in this age group. Indeed, most children will have developed some degree of immunity to pneumococcal disease as a result of natural exposure by 5 years of age, as is evidenced by the fact that pneumococcal disease is relatively rare in children over 5 years of age, even in the absence of infant vaccination. Thus, it is not unexpected that children from the 7vPnC and the MnCC groups in Study 3016 would have similar levels of pneumococcal IgG and OPA.

Assessor's comment: The response of the MAH is endorsed, and the explanation given considered plausible. Issue resolved.

QUESTION 2
There appears very little difference in quality and quantity of the immune response upon vaccination of both groups with Prevenar 13. The company is asked to comment on the apparent lack of anamnestic response, with regard to the 7vPnC serotypes, upon vaccination of the 7vPnC group with Prevenar 13.

Response
As discussed above, prior to entry into Study 3016, children in both vaccine groups had likely developed protective antibodies to a range of pneumococcal serotypes as a result of vaccination and/or natural exposure. Therefore, the similarity of the immune response in the 2 vaccine groups post-vaccination would not be unexpected.
The substantial response to a single vaccination of 13vPnC also reflects the status of the immune system among the children entering Study 3016. Because of the immaturity of the immune system in children less than 2 years of age, 2 to 3 doses of pneumococcal conjugate vaccine given by 6 months of age plus a booster dose in the second year of life are required to achieve protective and persistent antibody concentrations in this age group. However, by the time children are 11 to 14 years of age (the age of the subjects in Study 3016), the immune system has fully matured, such that a single dose

of pneumococcal conjugate vaccine should be sufficient to provide a robust and protective immune response. Indeed, this is what the immunogenicity results from Study 3016 demonstrate: ie, that among children in this age group, a single dose of 13vPnC is strongly immunogenic, regardless of prior vaccination with a pneumococcal conjugate vaccine.

Assessor's comment: The response of the MAH is endorsed and the explanation given considered plausible. Issue resolved.

3. Discussion on clinical aspects
No further data have been presented. The MAH has provided plausible explanations for the results seen in study 3016.

III. RAPPORTEUR'S OVERALL CONCLUSION AND RECOMMENDATION

- **Overall conclusion**
  All outstanding issues have been resolved.

- **Recommendation**

☒ **Fulfilled –**

No further action required

☐ **Not fulfilled:**

IV. ADDITIONAL CLARIFICATIONS REQUESTED

Not applicable