EMA/520305/2016

European Medicines Agency decision

P/0209/2016

of 12 August 2016

on the acceptance of a modification of an agreed paediatric investigation plan for pneumococcal polysaccharide serotype 6B conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein / Pneumococcal polysaccharide serotype 1 conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein / Pneumococcal polysaccharide serotype 18C conjugated to tetanus toxoid / Pneumococcal polysaccharide serotype 5 conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein / Pneumococcal polysaccharide serotype 19F conjugated to diphtheria toxoid / Pneumococcal polysaccharide serotype 14 conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein / Pneumococcal polysaccharide serotype 9V conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein / Pneumococcal polysaccharide serotype 4 conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein / Pneumococcal polysaccharide serotype 23F conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein / Pneumococcal polysaccharide serotype 7F conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein (Synflorix), (EMEA-000673-PIP01-09-M09) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

Disclaimer

This decision does not constitute entitlement to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006.

Only the English text is authentic.

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The European Medicines Agency,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No. 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004[1],

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency[2],

Having regard to the European Medicines Agency's decision P/104/2010 issued on 14 June 2010, the decision P/181/2011 issued on 28 July 2011, the decision P/232/2011 issued on 26 September 2011, the decision P/272/2011 issued on 28 October 2011, the decision P/0067/2012 issued on 30 March 2012, the decision P/0162/2012 issued on 23 July 2012, the decision P/0277/2012 issued on 21 November 2012, the decision P/0030/2014 issued on 21 February 2014 and the decision P/0270/2015 issued on 3 December 2015,

Having regard to the application submitted by GlaxoSmithKline Biologicals S.A. on 31 March 2016 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 24 June 2016, in accordance with Article 22 of Regulation (EC) No 1901/2006, and Article 21 of said Regulation and Article 13 of said Regulation,

[1] OJ L 378, 27.12.2006, p.1.
[2] OJ L 136, 30.4.2004, p. 1.

Having regard to Article 25 of Regulation (EC) No 1901/2006,

Whereas:

(1) The Paediatric Committee of the European Medicines Agency has given an opinion on the acceptance of changes to the agreed paediatric investigation plan and to the deferral.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan, including changes to the deferral.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for pneumococcal polysaccharide serotype 6B conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein / Pneumococcal polysaccharide serotype 1 conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein / Pneumococcal polysaccharide serotype 18C conjugated to tetanus toxoid / Pneumococcal polysaccharide serotype 5 conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein / Pneumococcal polysaccharide serotype 19F conjugated to diphtheria toxoid / Pneumococcal polysaccharide serotype 14 conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein / Pneumococcal polysaccharide serotype 9V conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein / Pneumococcal polysaccharide serotype 4 conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein / Pneumococcal polysaccharide serotype 23F conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein / Pneumococcal polysaccharide serotype 7F conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein, (Synflorix), suspension for injection, intramuscular use, including changes to the deferral, are hereby accepted in the scope set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices.

Article 2

This decision is addressed to GlaxoSmithKline Biologicals S.A., Rue de l'Institut 89, 1330 – Rixensart, Belgium.

EMA/PDCO/262320/2016
London, 24 June 2016

Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan

EMEA-000673-PIP01-09-M09

Scope of the application

Active substance(s):

Pneumococcal polysaccharide serotype 6B conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein / Pneumococcal polysaccharide serotype 1 conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein / Pneumococcal polysaccharide serotype 18C conjugated to tetanus toxoid / Pneumococcal polysaccharide serotype 5 conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein / Pneumococcal polysaccharide serotype 19F conjugated to diphtheria toxoid / Pneumococcal polysaccharide serotype 14 conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein / Pneumococcal polysaccharide serotype 9V conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein / Pneumococcal polysaccharide serotype 4 conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein / Pneumococcal polysaccharide serotype 23F conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein / Pneumococcal polysaccharide serotype 7F conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein

Invented name:

Synflorix

Condition(s):

Prevention of diseases caused by streptococcus pneumoniae

Prevention of acute otitis media caused by non-typeable Haemophilus influenzae

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Suspension for injection

Route(s) of administration:

Intramuscular use

Name/corporate name of the PIP applicant:

GlaxoSmithKline Biologicals S.A.

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, GlaxoSmithKline Biologicals S.A. submitted to the European Medicines Agency on 31 March 2016 an application for modification of the agreed paediatric investigation plan with a deferral and a waiver as set out in the European Medicines Agency's decision P/104/2010 issued on 14 June 2010, the decision P/181/2011 issued on 28 July 2011, the decision P/232/2011 issued on 26 September 2011, the decision P/272/2011 issued on 28 October 2011, the decision P/0067/2012 issued on 30 March 2012, the decision P/0162/2012 issued on 23 July 2012, the decision P/0277/2012 issued on 21 November 2012, the decision P/0030/2014 issued on 21 February 2014 and the decision P/0270/2015 issued on 3 December 2015.

The application for modification proposed changes to the agreed paediatric investigation plan and to the deferral.

The procedure started on 26 April 2016.

Scope of the modification

Some timelines of the Paediatric Investigation Plan have been modified.

Opinion

1. The Paediatric Committee, having assessed the application in accordance with Article 22 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree to changes to the paediatric investigation plan and to the deferral in the scope set out in the Annex I of this opinion.

   The Norwegian Paediatric Committee member agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the paediatric investigation plan and the subset(s) of the paediatric population and condition(s) covered by the waiver are set out in the Annex I.

This opinion is forwarded to the applicant and the Executive Director of the European Medicines Agency, together with its annexes and appendix.

Annex I

The subset(s) of the paediatric population and condition(s) covered by the waiver and the measures and timelines of the agreed paediatric investigation plan (PIP)

1. Waiver

1.1. Condition: prevention of diseases caused by streptococcus pneumoniae

The waiver applies to:

- the paediatric population from birth to less than 6 weeks of age;
- for suspension for injection for intramuscular use;
- on the grounds that the specific medicinal product is likely to be ineffective.

1.2. Condition: prevention of acute otitis media caused by haemophilus influenzae

The waiver applies to:

- the paediatric population from birth to less than 6 weeks of age;
- for suspension for injection for intramuscular use;
- on the grounds that the specific medicinal product is likely to be ineffective.

2. Paediatric Investigation Plan

2.1. Condition: prevention of diseases caused by streptococcus pneumoniae

2.1.1. Indication(s) targeted by the PIP

Active immunisation against disease caused by streptococcus pneumoniae serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (including sepsis, meningitis, pneumonia, bacteraemia and acute otitis media)

2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From 6 weeks to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Suspension for injection for intramuscular use.

2.1.4. Studies

Area	Number of studies	Description
Quality related studies		Not applicable.

Non-clinical studies		Not applicable.
Clinical studies	10	**Study 1)** 109563 (10PN-PD-DIT-028) Observer-blind, randomized, controlled, multicentre study to evaluate the efficacy of Synflorix against community acquired pneumonia and acute otitis media. **Study 2)** 112595 (10PN-PD-DIT-053) Double-blind, cluster-randomized, controlled study to evaluate the impact on nasopharyngeal carriage, acute otitis media, immunogenicity and safety of S in children starting vaccination below 19 months of age. **Study 3)** 10PN-PD-DIT-034 PRI & BST Open label, controlled study in South Africa to evaluate the immunogenicity, safety and reactogenicity of Synflorix administered as a 3-dose primary immunization course in HIV infected infants, HIV exposed uninfected infants and HIV unexposed uninfected infants. **Study 4)** 10PN-PD-DIT-042 EXT 014 Long-term follow-up study to assess the immune responses following vaccination with a booster dose of Synflorix and to evaluate the immunogenicity and safety of a 2-dose catch-up immunization course with Synflorix in the fourth year of life. **Study 5)** 10PN-PD-DIT-043 Cluster-randomized, controlled study to evaluate the effectiveness of Synflorix in reducing the incidence of invasive diseases. **Study 6)** 10PN-PD-DIT-041 EXT-007 Y1, Y2, Y4 Long-term follow-up study to evaluate antibody persistence and immunological memory in children previously vaccinated with four doses of Synflorix in primary vaccination study 10PN-PD-DIT-001 and booster vaccination study 10PN-PD-DIT-007 and assessment of immune responses following a 2-dose catch-up immunization with Synflorix.

		Study 7) 10PN-PD-DIT-046 EXT:002 Long-term follow-up study to assess the immune responses following vaccination with a booster dose of 10-valent pneumococcal conjugate vaccine (Synflorix) and to evaluate the immunogenicity and safety of a 2-dose catch-up immunization course with Synflorix. **Study 8)** 10PN-PD-DIT-062 Open, controlled study in children previously enrolled in study 10PN-PD-DIT-037 to assess the immunogenicity, safety and reactogenicity of 10-valent pneumococcal conjugate vaccine (Synflorix) when administered as a booster dose at either 9-12 or 15-18 months of age in primed children or when administered as a catch-up vaccination (2+1 schedule) in unprimed children during the second year of life. **Study 9)** 10PN-PD-DIT-064 Open, controlled study to evaluate immunogenicity, safety and reactogenicity of Synflorix administered intramuscularly to sickle cell disease subjects from 8 weeks to less than 2 years of age, as compared to age-matched healthy subjects. **Study 10)** 10PN-PD-DIT-072 Open-label, controlled study to evaluate immunogenicity, safety and reactogenicity of 10-valent pneumococcal conjugate vaccine administered to children aged from 2 to less than 18 years who are at an increased risk of pneumococcal infection and to a control group of healthy children aged from 24 to 59 months.

2.2. Condition: Prevention of acute otitis media caused by non-typeable Haemophilus influenzae.

2.2.1. Indication(s) targeted by the PIP

Active immunisation against acute otitis media caused by non-typeable Haemophilus influenzae.

2.2.2. Subset(s) of the paediatric population concerned by the paediatric development

From 6 weeks to less than 18 years of age

2.2.3. Pharmaceutical form(s)

Suspension for injection for intramuscular use

2.2.4. Studies

Area	Number of studies	Description
Quality related studies		Not applicable.
Non-clinical studies		Not applicable.
Clinical studies	4	**Study 1)** 109563 (10PN-PD-DIT-028) Observer-blind, randomized, controlled, multicentre study to evaluate the efficacy of Synflorix against community acquired pneumonia and acute otitis media. (same study as for the condition “prevention of diseases caused by streptococcus pneumoniae”) **Study 2)** 112595 (10PN-PD-DIT-053) Cluster-randomized, controlled study to evaluate the effectiveness of Synflorix against community acquired pneumonia and occurrence of tympanostomy tube placement, and nasopharyngeal carriage of Streptococcus pneumonia serotypes and Haemophilus influenzae. (same study as for the condition “prevention of diseases caused by streptococcus pneumoniae”) **Study 4)** 10PN-PD-DIT-042 EXT 014 Long-term follow-up study to assess the immune responses following vaccination with a booster dose of Synflorix and to evaluate the immunogenicity and safety of a 2-dose catch-up immunization course with Synflorix in the fourth year of life. (same study as for the condition “prevention of diseases caused by streptococcus pneumoniae”) **Study 5)** 10PN-PD-DIT-043 Cluster-randomized, controlled study to evaluate the effectiveness of Synflorix in reducing the incidence of invasive diseases. (same study as for the condition “prevention of diseases caused by streptococcus pneumoniae”)

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety/efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	By December 2016
Deferral for one or more studies contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

1. Prevention of diseases caused by *streptococcus pneumoniae*

Authorised indication(s):

- Active immunisation against invasive disease, pneumonia and acute otitis media caused by Streptococcus pneumoniae in infants and children from 6 weeks up to 5 years of age.

Authorised pharmaceutical form(s):

Suspension for injection

Authorised route(s) of administration:

Intramuscular use