EMA/763267/2011

European Medicines Agency decision

P/232/2011

of 26 September 2011

on the acceptance of a modification of an agreed paediatric investigation plan for pneumococcal polysaccharide serotype 1 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 5 conjugated to protein D (derived from non-typeable haemophilus influenzae) carrier protein / pneumococcal polysaccharide serotype 6B 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 / pneumococcal polysaccharide serotype 9V conjugated to protein D (derived from non-typeable haemophilus influenzae) carrier protein / pneumococcal polysaccharide serotype 14 conjugated to protein D (derived from non-typeable haemophilus influenzae) carrier protein / pneumococcal polysaccharide serotype 18C conjugated to tetanus toxoid / pneumococcal polysaccharide serotype 19F conjugated to diphtheria toxoid / pneumococcal polysaccharide serotype 23F conjugated to protein D (derived from non-typeable haemophilus influenzae) carrier protein (Synflorix), (EMEA-000673-PIP01-09-M02) 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.

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8409
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

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on the acceptance of a modification of an agreed paediatric investigation plan for pneumococcal polysaccharide serotype 1 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 5 conjugated to protein D (derived from non-typeable haemophilus influenzae) carrier protein / pneumococcal polysaccharide serotype 6B 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 / pneumococcal polysaccharide serotype 9V conjugated to protein D (derived from non-typeable haemophilus influenzae) carrier protein / pneumococcal polysaccharide serotype 14 conjugated to protein D (derived from non-typeable haemophilus influenzae) carrier protein / pneumococcal polysaccharide serotype 18C conjugated to tetanus toxoid / pneumococcal polysaccharide serotype 19F conjugated to diphtheria toxoid / pneumococcal polysaccharide serotype 23F conjugated to protein D (derived from non-typeable haemophilus influenzae) carrier protein (Synflorix), (EMEA-000673-PIP01-09-M02) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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 and the decision P/181/2011 issued on 28 July 2011,

Having regard to the application submitted by GlaxoSmithKline Biologicals S.A. on 29 July 2011 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 9 September 2011, in accordance with Article 22 of Regulation (EC) No 1901/2006,

[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.

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

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for pneumococcal polysaccharide serotype 1 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 5 conjugated to protein D (derived from non-typeable haemophilus influenzae) carrier protein / pneumococcal polysaccharide serotype 6B 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 / pneumococcal polysaccharide serotype 9V conjugated to protein D (derived from non-typeable haemophilus influenzae) carrier protein / pneumococcal polysaccharide serotype 14 conjugated to protein D (derived from non-typeable haemophilus influenzae) carrier protein / pneumococcal polysaccharide serotype 18C conjugated to tetanus toxoid / pneumococcal polysaccharide serotype 19F conjugated to diphtheria toxoid / pneumococcal polysaccharide serotype 23F conjugated to protein D (derived from non-typeable haemophilus influenzae) carrier protein (Synflorix), suspension for injection, intramuscular use, 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.

Done at London, 26 September 2011

For the European Medicines Agency
Andreas Pott
Acting Executive Director
(Signature on file)

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

EMEA-000673-PIP01-09-M02

Scope of the application

Active substance(s):

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

Invented name:

Synflorix

Condition(s):

Diseases caused by streptococcus pneumoniae

Acute otitis media caused by 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 29 July 2011 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 and the decision P/181/2011 issued on 28 July 2011.

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

The procedure started on 16 August 2011.

Scope of the modification

Some measures and timelines of the original Opinion 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 in the scope set out in the Annex I of this opinion.

   The Icelandic and the Norwegian Paediatric Committee members agree 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 annex(es) and appendix.

London, 9 September 2011

On behalf of the Paediatric Committee
Dr Daniel Brasseur, Chairman
(Signature on file)

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

1. Waiver

1.1. Condition: Disease 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: 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 to be investigated: Diseases caused by Streptococcus pneumoniae.

2.1.1. Indication 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		Not applicable.
Non-clinical		Not applicable.
Clinical	10	Study 1) 109563 (10PN-PD-DIT-028) Double-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 18 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-

Area	Number of studies	Description
		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, controlled study to evaluate immunogenicity of Synflorix administered intramuscularly to asplenic subjects from 2 to less than 18 years of age, as compared to age-matched non-asplenic subjects.

2.2. Condition to be investigated: Acute otitis media caused by non-typeable Haemophilus influenzae.

2.2.1. Indication 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		Not applicable.
Non-clinical		Not applicable.
Clinical	4	Study 1) 109563 (10PN-PD-DIT-028) Double-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) Cluster-randomized, controlled study to evaluate the effectiveness of

Area	Number of studies	Description
		Synflorix against community acquired pneumonia and occurrence of tympanostomy tube placement, and nasopharyngeal carriage of Streptococcus pneumonia serotypes and Haemophilus influenzae. 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.

3. Follow-up, completion and deferral of pip

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	By September 2014
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):

Diseases caused by streptococcus pneumoniae

Authorised indication: Active immunisation against invasive disease and acute otitis media caused by Streptococcus pneumoniae in infants and children from 6 weeks up to 2 years of age.

EU Number	(Invented) name	Strength	Pharmaceutical Form	Route of Administration	Packaging	Content (concentration)	Package size
EU/1/09/508/001	Synflorix	- -	Suspension for injection	Intramuscular use	pre-filled syringe (glass)	0.5 ml	1 pre-filled syringe
EU/1/09/508/002	Synflorix	- -	Suspension for injection	Intramuscular use	pre-filled syringe (glass)	0.5 ml	10 pre-filled syringes
EU/1/09/508/003	Synflorix	- -	Suspension for injection	Intramuscular use	pre-filled syringe (glass)	0.5 ml	1 pre-filled syringe + 1 needle
EU/1/09/508/004	Synflorix	- -	Suspension for injection	Intramuscular use	pre-filled syringe (glass)	0.5 ml	10 pre-filled syringes + 10 needles
EU/1/09/508/005	Synflorix	- -	Suspension for injection	Intramuscular use	pre-filled syringe (glass)	0.5 ml	1 pre-filled syringe + 2 needles
EU/1/09/508/006	Synflorix	- -	Suspension for injection	Intramuscular use	vial (glass)	0.5 ml	1 vial
EU/1/09/508/007	Synflorix	- -	Suspension for injection	Intramuscular use	vial (glass)	0.5 ml	10 vials

EU Number	(Invented) name	Strength	Pharmaceutical Form	Route of Administration	Packaging	Content (concentration)	Package size
EU/1/09/508/008	Synflorix	- -	Suspension for injection	Intramuscular use	vial (glass)	0.5 ml	100 vials
EU/1/09/508/009	Synflorix	- -	Suspension for injection	Intramuscular use	vial (glass)	1.0 ml	100 vials (multidose)
EU/1/09/508/010	Synflorix	- -	Suspension for injection	Intramuscular use	pre-filled syringe (glass)	0.5 ml	50 pre-filled syringes