Synflorix

Summary of Product Characteristics

1. Name of the medicinal product

Synflorix suspension for injection in pre-filled syringe

Synflorix suspension for injection

Synflorix suspension for injection in multidose container (2 doses)

Synflorix suspension for injection in multidose container (4 doses)

Pneumococcal polysaccharide conjugate vaccine (adsorbed)

2. Qualitative and quantitative composition

1 dose (0.5 ml) contains:

Component	Amount
Pneumococcal polysaccharide serotype 1[1],[2]	1 microgram
Pneumococcal polysaccharide serotype 4[1],[2]	3 micrograms
Pneumococcal polysaccharide serotype 5[1],[2]	1 microgram
Pneumococcal polysaccharide serotype 6B[1],[2]	1 microgram
Pneumococcal polysaccharide serotype 7F[1],[2]	1 microgram
Pneumococcal polysaccharide serotype 9V[1],[2]	1 microgram
Pneumococcal polysaccharide serotype 14[1],[2]	1 microgram
Pneumococcal polysaccharide serotype 18C[1],[3]	3 micrograms
Pneumococcal polysaccharide serotype 19F[1],[4]	3 micrograms
Pneumococcal polysaccharide serotype 23F[1],[2]	1 microgram

[1] adsorbed on aluminium phosphate — 0.5 milligram Al^{3+} in total

[2] conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein — 9–16 micrograms

[3] conjugated to tetanus toxoid carrier protein — 5–10 micrograms

[4] conjugated to diphtheria toxoid carrier protein — 3–6 micrograms

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Suspension for injection (injection). The vaccine is a turbid white suspension.

4. Clinical particulars

4.1 Therapeutic indications

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. See sections 4.4 and 5.1 for information on protection against specific pneumococcal serotypes.

The use of Synflorix should be determined on the basis of official recommendations taking into consideration the impact on pneumococcal diseases in different age groups as well as the variability of the epidemiology in different geographical areas.

4.2 Posology and method of administration

Posology

The immunisation schedules for Synflorix should be based on official recommendations. It is recommended that individuals who receive a first dose of Synflorix complete the full vaccination course with Synflorix.

Infants from 6 weeks to 6 months of age

Three-dose primary series: The recommended immunisation series to ensure optimal protection consists of four doses, each of 0.5 ml. The primary infant series consists of three doses with the first dose usually given at 2 months of age and with an interval of at least 1 month between doses. The first dose may be given as early as 6 weeks of age. A booster (fourth) dose is recommended at least 6 months after the last primary dose and may be given from the age of 9 months onwards (preferably between 12 and 15 months of age) (see sections 4.4 and 5.1).

Two-dose primary series: Alternatively, when Synflorix is given as part of a routine infant immunisation programme, a series consisting of three doses, each of 0.5 ml, may be given. The first dose may be given as early as 6 weeks of age with a second dose administered 2 months later. A booster (third) dose is recommended at least 6 months after the last primary dose and may be given from the age of 9 months onwards (preferably between 12 and 15 months of age) (see section 5.1).

Preterm newborn infants (born between 27–36 weeks gestation): In preterm infants born after at least 27 weeks of gestational age, the recommended immunisation series consists of four doses, each of 0.5 ml. The primary infant series consists of three doses with the first dose given at 2 months of age and with an interval of at least 1 month between doses. A booster (fourth) dose is recommended at least 6 months after the last primary dose (see sections 4.4 and 5.1).

Unvaccinated infants and children ≥ 7 months of age: Infants aged 7–11 months: two primary doses of 0.5 ml with an interval of at least 1 month between doses, followed by a booster (third) dose in the second year of life with an interval of at least 2 months after the last primary dose. Children aged 12 months–5 years: two doses of 0.5 ml with an interval of at least 2 months between doses.

Special populations: In individuals with underlying conditions predisposing them to invasive pneumococcal disease (such as HIV infection, sickle cell disease (SCD) or splenic dysfunction), Synflorix may be given according to the above schedules except that a 3-dose schedule should be given as primary vaccination in infants starting vaccination from 6 weeks to 6 months of age (see sections 4.4 and 5.1).

Paediatric population: The safety and efficacy of Synflorix in children over 5 years of age have not been established.

Use of Synflorix and other pneumococcal conjugate vaccines: Limited clinical data are available on the use of both Synflorix and 13-valent pneumococcal conjugate vaccine (PCV13) in the immunisation course of an individual (see section 5.1).

Method of administration: The vaccine should be given by intramuscular injection. The preferred sites are the anterolateral aspect of the thigh in infants or the deltoid muscle of the upper arm in young children.

4.3 Contraindications

Hypersensitivity to the active substances or to any of the excipients listed in section 6.1, or to any of the carrier proteins.

As with other vaccines, the administration of Synflorix should be postponed in subjects suffering from acute severe febrile illness. However, the presence of a minor infection, such as a cold, should not result in the deferral of vaccination.

4.4 Special warnings and precautions for use

Traceability: In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Prior to immunisation: As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic reaction following administration. The potential risk of apnoea and the need for respiratory monitoring for 48–72 h should be considered when administering the primary immunisation series to very premature infants (born ≤ 28 weeks of gestation), particularly those with a previous history of respiratory immaturity; as the benefit of vaccination is high in this group, vaccination should not be withheld or delayed.

Synflorix should under no circumstances be administered intravascularly or intradermally. No data are available on subcutaneous administration.

In children as of 2 years of age, syncope (fainting) can occur following, or even before, any vaccination as a psychogenic response to the needle injection; procedures should be in place to avoid injury from faints.

As for other vaccines administered intramuscularly, Synflorix should be given with caution to individuals with thrombocytopenia or any coagulation disorder since bleeding may occur following intramuscular administration.

Information on protection conferred by the vaccine: Official recommendations for the immunisation against diphtheria, tetanus and Haemophilus influenzae type b should also be followed. There is insufficient evidence that Synflorix provides protection against pneumococcal serotypes not contained in the vaccine except the cross-reactive serotype 19A, or against non-typeable Haemophilus influenzae; Synflorix does not provide protection against other micro-organisms. As with any vaccine, Synflorix may not protect all vaccinated individuals against invasive pneumococcal disease, pneumonia or otitis media caused by the vaccine serotypes and serotype 19A. Because otitis media and pneumonia are caused by many micro-organisms other than the represented serotypes, overall protection against these diseases is expected to be limited and substantially lower than protection against invasive disease.

In clinical trials, Synflorix elicited an immune response to all ten serotypes, but the magnitude varied; the functional immune response to serotypes 1 and 5 was lower in magnitude than the response against other vaccine serotypes, and it is not known whether this will result in lower protective efficacy against invasive disease, pneumonia or otitis media caused by these serotypes.

Children should receive the dose regimen appropriate to their age at the time of commencing the vaccination series (see section 4.2).

Immunosuppressive therapy and immunodeficiency: Children with impaired immune responsiveness (due to immunosuppressive therapy, a genetic defect, HIV infection, prenatal exposure to anti-retroviral therapy and/or HIV, or other causes) may have reduced antibody response to vaccination. Safety and immunogenicity data are available for HIV infected infants, HIV negative infants born from HIV positive mothers, children with sickle cell disease and children with splenic dysfunction (see sections 4.8 and 5.1); data are not available for other specific immunocompromised groups and vaccination should be considered on an individual basis.

The use of pneumococcal conjugate vaccine does not replace the use of 23-valent pneumococcal polysaccharide vaccines in children ≥2 years of age at higher risk for invasive disease. Whenever recommended, at-risk children ≥24 months already primed with Synflorix should receive the 23-valent polysaccharide vaccine, with an interval of not less than 8 weeks.

Prophylactic use of antipyretics: Prophylactic administration of antipyretics before or immediately after vaccination can reduce the incidence and intensity of post-vaccination febrile reactions. Clinical data suggest prophylactic paracetamol might reduce the fever rate (and might reduce the immune response to Synflorix, though the clinical relevance is unknown), while prophylactic ibuprofen showed a limited effect. The use of prophylactic antipyretics is

recommended for all children receiving Synflorix simultaneously with whole cell pertussis vaccines, and for children with seizure disorders or a prior history of febrile seizures.

Sodium content: This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Use with other vaccines: Synflorix can be given concomitantly with any of the following monovalent or combination vaccines (including DTPa-HBV-IPV/Hib and DTPw-HBV/Hib): diphtheria-tetanus-acellular pertussis vaccine (DTPa), hepatitis B vaccine (HBV), inactivated polio vaccine (IPV), Haemophilus influenzae type b vaccine (Hib), diphtheria-tetanus-whole cell pertussis vaccine (DTPw), measles-mumps-rubella vaccine (MMR), varicella vaccine (V), meningococcal serogroup C conjugate vaccine, meningococcal serogroups A, C, W-135 and Y conjugate vaccine, oral polio vaccine (OPV) and oral rotavirus vaccine. Different injectable vaccines should always be given at different injection sites.

Clinical studies demonstrated that immune responses and safety profiles of co-administered vaccines were unaffected, with the exception of the inactivated poliovirus type 2 response (inconsistent results across studies, seroprotection ranging from 78% to 100%). When the meningococcal ACWY vaccine was co-administered with a Synflorix booster in the second year of life, lower antibody GMC and OPA GMT were observed for serotype 18C, with no impact on the other nine serotypes; enhancement of antibody response to Hib-TT conjugate, diphtheria and tetanus antigens was observed. Clinical relevance of these observations is unknown.

Use with systemic immunosuppressive medicinal products: As with other vaccines, an adequate response may not be elicited in patients receiving immunosuppressive treatment.

Use with prophylactic administration of antipyretics: Clinical data suggest prophylactic paracetamol might reduce the immune response to Synflorix; clinical relevance is unknown (see section 4.4).

4.6 Fertility, pregnancy and lactation

Synflorix is not intended for use in adults. Human data on use during pregnancy or breast-feeding and animal reproduction studies are not available.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

Summary of the safety profile

Safety assessment of Synflorix was based on clinical trials involving the administration of 63,905 doses to 22,429 healthy children and 137 preterm infants as primary vaccination; 19,466 children and 116 preterm infants received a booster dose in the second year of life. Safety was also assessed in 435 previously unvaccinated children 2 to 5 years old, of whom 285 received 2 doses. In all trials, Synflorix was administered concurrently with recommended childhood vaccines.

In infants, the most common adverse reactions after primary vaccination were redness at the injection site and irritability (approximately 41% and 55% of all doses respectively). Following booster vaccination, the most common reactions were pain at the injection site and irritability (approximately 51% and 53% respectively). Most reactions were mild to moderate and not long lasting; no increase in incidence or severity was seen with subsequent primary doses.

Local reactogenicity was similar in infants <12 months and children >12 months, except for injection site pain, which increased with age (>39% in infants <12 months vs >58% in children >12 months). Following booster vaccination, children >12 months are more likely to experience injection site reactions than infants during the primary series. Following catch-up vaccination in children 12–23 months, urticaria was reported more frequently (uncommon) than in infants during primary and booster vaccination.

Reactogenicity was higher in children receiving whole cell pertussis vaccines concomitantly; after the primary course, fever ≥38°C and >39°C was reported in 86.1% and 14.7% of children receiving Synflorix with DTPw, versus 82.9% and 11.6% with 7-valent Prevenar. In comparative clinical studies, the incidence of local and general adverse events reported within 4 days after each dose was within the same range as after 7-valent Prevenar.

Tabulated list of adverse reactions

Frequencies: Very common (≥1/10); Common (≥1/100 to <1/10); Uncommon (≥1/1,000 to <1/100); Rare (≥1/10,000 to <1/1,000); Very rare (<1/10,000). Within each frequency grouping, reactions are presented in order of decreasing seriousness.

System Organ Class	Frequency	Adverse reactions
Clinical trials		
Immune system disorders	Rare	Allergic reactions (such as eczema, allergic dermatitis, atopic dermatitis)
	Very rare	Angioedema
Metabolism and nutrition disorders	Very common	Appetite lost
Psychiatric disorders	Very common	Irritability

System Organ Class	Frequency	Adverse reactions
	Uncommon	Crying abnormal
Nervous system disorders	Very common	Drowsiness
	Rare	Convulsions (including febrile convulsions)
Vascular disorders	Very rare	Kawasaki disease
Respiratory, thoracic and mediastinal disorders	Uncommon	Apnoea in very premature infants (≤28 weeks of gestation) (see section 4.4)
Gastrointestinal disorders	Uncommon	Diarrhoea, vomiting
Skin and subcutaneous tissue disorders	Uncommon	Rash
	Rare	Urticaria
General disorders and administration site conditions	Very common	Fever ≥38°C rectally (age <2 years), pain, redness, swelling at the injection site
	Common	Fever >39°C rectally (age <2 years), injection site reactions like induration
	Uncommon	Injection site reactions like haematoma, haemorrhage and nodule
Adverse reactions additionally reported after booster vaccination of primary series and/or catch-up vaccination		
Nervous system disorders	Uncommon	Headache (age 2 to 5 years)
Gastrointestinal disorders	Uncommon	Nausea (age 2 to 5 years)
General disorders and administration site conditions	Common	Fever ≥38°C rectally (age 2 to 5 years)
	Uncommon	Fever >40°C rectally (age <2 years), fever >39°C rectally (age 2 to 5 years), injection site reactions like diffuse swelling of the injected limb, sometimes involving the adjacent joint, pruritus
Post-marketing experience		
Immune system disorders	Very rare	Anaphylaxis
Nervous system disorders	Rare	Hypotonic-hyporesponsive episode

Special populations: Safety of Synflorix was assessed in 83 HIV positive infants, 101 HIV negative infants born from HIV positive mothers, and 50 infants with sickle cell disease (SCD) receiving primary vaccination (76, 96 and 49 respectively received a booster dose); also in 50 children with SCD starting vaccination at 7–11 months of age (all receiving booster vaccination) and 50

children with SCD starting vaccination at 12–23 months of age. Results suggest comparable reactogenicity and safety profile between these high risk groups and healthy children.

Reporting of suspected adverse reactions: Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

No case of overdose has been reported.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: vaccines, pneumococcal vaccines, ATC code: J07AL52

Extensive clinical data support the efficacy and immunogenicity of Synflorix against invasive pneumococcal disease, pneumonia, acute otitis media, and nasopharyngeal carriage, including large-scale randomised controlled trials (FinIP, COMPAS, POET) and post-marketing effectiveness surveillance in Brazil, Finland and Quebec. Vaccine effectiveness/efficacy against culture-confirmed invasive pneumococcal disease (IPD) due to vaccine serotypes ranged from 66.7% to 100% depending on schedule and study. Efficacy against likely bacterial community-acquired pneumonia was demonstrated (interim analysis vaccine efficacy of 22.0%, 95% CI: 7.7; 34.2). Efficacy against clinical and pneumococcal acute otitis media, and immunogenicity data (including non-inferiority to 7-valent Prevenar, immune memory, and immunogenicity in preterm infants and special populations such as HIV-exposed/infected infants, children with sickle cell disease, and children with splenic dysfunction) are described in detail in the full prescribing information. Synflorix induces an immune response to the cross-reactive serotype 19A. The clinical relevance of certain differences in immune response magnitude between serotypes (in particular serotypes 1, 5, 6B and 23F) has not been fully established, though effectiveness against IPD caused by serotype 6B has been demonstrated.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Studies with an 11-valent vaccine formulation representative for Synflorix revealed no special hazard for humans based on conventional studies of safety pharmacology, single and repeated dose toxicity.

6. Pharmaceutical particulars

6.1 List of excipients

1-dose and 2-dose containers: Sodium chloride; Water for injections

4-dose container: Sodium chloride; 2-phenoxyethanol; Water for injections

For adsorbent, see section 2.

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

1-dose and 2-dose containers: 4 years

4-dose container: 3 years

After first opening of multidose vial:

2-dose vial: Immediate use is recommended. If not used immediately, store in a refrigerator (2°C–8°C); discard if not used within 6 hours.

4-dose vial: May be stored for a maximum of 28 days in a refrigerator (2°C–8°C); discard if not used within 28 days.

6.4 Special precautions for storage

Store in a refrigerator (2°C–8°C). Do not freeze. Store in the original package in order to protect from light.

6.5 Nature and contents of container

Pre-filled syringe: 0.5 ml of suspension in a pre-filled syringe (type I glass) with a plunger stopper (butyl rubber) and a rubber tip cap. Pack sizes of 1, 10 and 50, with or without needles.

Vial: 0.5 ml of suspension in a vial (type I glass) for 1 dose with a stopper (butyl rubber). Pack sizes of 1, 10 and 100.

Multidose vial: 1 ml of suspension in a vial (type I glass) for 2 doses with a stopper (butyl rubber), pack size of 100. 2 ml of suspension in a vial (type I glass) for 4 doses with a stopper (butyl rubber), pack sizes of 10 and 100.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

A fine white deposit with a clear colourless supernatant may be observed upon storage of the pre-filled syringe or vial; this does not constitute a sign of

deterioration. The content should be inspected visually both before and after shaking for any foreign particulate matter and/or abnormal physical appearance prior to administration; discard the vaccine if either is observed. The vaccine should be allowed to reach room temperature before use and should be well shaken before use. When using a multidose vial, each 0.5 ml dose should be withdrawn using a sterile needle and syringe, with precautions taken to avoid contamination of the contents.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing authorisation holder

GlaxoSmithKline Biologicals S.A., Rue de l'Institut 89, B-1330 Rixensart, Belgium

8. Marketing authorisation number(s)

H2009/19797/274/R1

9. Date of first authorisation/renewal of the authorisation

2026 August 23

10. Date of revision of the text

2026 August 23