Unit: Technical Assessment Unit

Public assessment report for biological products

(Prevenar 13)

Administrative information:

Trade name of the medicinal product:	Prevenar 13 suspension for injection
INN (or common name) of the active substance(s):	Pneumococcal polysaccharide serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F **conjugated** to CRM_{197} carrier protein and adsorbed on aluminum phosphate (0.125 mg aluminum)
Manufacturer of the finished product	Pfizer Manufacturing Belgium NV, Rijksweg 12, 2870 Puurs, Belgium
Marketing Authorization holder	Pfizer –Egypt
Applied Indication(s):	Active immunization for the prevention of invasive disease, pneumonia and acute otitis media caused by Streptococcus pneumoniae in infants, children and adolescents from 6 weeks to 17 years of age. Active immunization for the prevention of invasive disease and pneumonia caused by Streptococcus pneumoniae in adults ≥18 years of age and the elderly.
Pharmaceutical form(s) and strength(s):	Suspension for injection in a pre-filled syringe 0.5ml. Each 0.5ml dose contains 2.2 mcg of each serotype (1, 3, 4, 5, 6A, 7F, 9V, 14, 18C, 19A, 19F, 23F) 4.4 mcg of serotype 6B
Route of administration	Intramuscular injection
Type of registration (EMA/FDA – Local)	EMA approved

List of abbreviations

13vPnC: Prevenar 13
2-PE: 2-phenoxyethanol
AlPO4: Aluminum Phosphate
CRM197: cross-reactive material 197
EEA: European Economic Area
EMA: European Medicines Agency
GMC: Geometric Mean concentration
IgG: immunoglobulin G
IM: Intramuscular
LLOQ: Lower Limit of Quantification
MA: Marketing Authorization
MDV: Multi Dose Vial
NZW: New Zealand White rabbit
OPA: Opsonophagocytic activity
P80: polysorbate 80
PFS: pre-filled syringe
Ph.Eur: European Pharmacopoeia
SDS: single-dose prefilled syringe
WHO: World Health Organization

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Dossier initial submission and evaluation process:

The file evaluated according to normal track pathway & the company submitted data which are the Quality module-3 from the CTD file.

1. **General introduction about the product including brief description of the AI, its mode of action and indications.**

Prevenar 13, is a 13-valent pneumococcal conjugate vaccine (13vPnC) for use in infants and young children to prevent pneumococcal disease (invasive pneumococcal disease [IPD], non bacteremic pneumonia, and acute otitis media [AOM]) caused by the 13 serotypes contained in the vaccine.
. The 13-valent vaccine is a sterile suspension of saccharides of the capsular antigens of *Streptococcus pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F, individually linked to non-toxic diphtheria CRM197 protein.

The recommended dosing regimen for prevenar 13 is a single dose of 0.5 ml.

Each 0.5 mL dose of the vaccine is formulated to contain approximately 2.2 µg of each of *Streptococcus pneumoniae* serotypes, 4.4 µg of 6B saccharides, 34 µg CRM197 carrier protein, 100 µg polysorbate 80, 295 µg succinate buffer and 0.125 mg of aluminum as aluminum phosphate adjuvant with 4 mg of 2-PE.

2. **Quality aspects:**

- **Introduction**

As mentioned in the aforementioned section.

3. **Drug substance:**

Manufacturer:

Wyeth biopharmaceutical Division of Wyeth pharmaceutical LLC. 1 Burtt Road, Andover MA 01810, USA is Holdings Corporation-USA manufacture of pneumococcal saccharides

Stability

The results of stability studies for three production batches of DS component support the claimed shelf-life when stored in its proper container.

2.2.3 Drug product:

- **Manufacturer of the drug product:**
  Manufacturer of finished products and 1ry Packaging:

Pfizer pharmaceutical, Grange Castle Business Park, Clondalkin, Dublin 22- Ireland
Manufacturer responsible for secondary packaging and batch release:
Pfizer Manufacturing Belgium NV, Rijksweg 12, 2870 Puurs, Belgium

- **Stability of Drug product**
  Approved shelf life for the finished product: 3 years
  Approved Storage Conditions of the finished product: - Store in a refrigerator (2 °C – 8 °C). Do not freeze. Prevenar 13is stable at temperature up to 25 °C for 4 days.

4. Non–clinical aspect:

The 13-valent pneumococcal conjugate vaccine (13vPnC, Prevenar 13) contains polysaccharides from the pneumococcal serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F, all individually conjugated to cross-reactive material 197 (CRM197). Prevenar 13 is available in a single-dose pre-filled syringe (PFS). Each dose is formulated to contain 2.2 µg per serotype, except for 4.4 mg of 6B. While each 0.5-mL dose is formulated in 5 mM succinate buffer with 0.85% sodium chloride (NaCl) at pH 5.8, with 0.125 mg of aluminum as aluminum phosphate ($AlPO_4$) and 0.02% polysorbate 80 (P80) as excipients and there is no preservative in this single-dose formulation. A formulation has now been developed, for use in the developing world, which uses the same formulation as the licensed 13vPnC (described above) with 2-phenoxyethanol (2-PE) added as a preservative, and filled into multidose vials.

Pharmacology:

In the immunogenicity study in cynomolgus monkeys, the 13vPnC with 2-PE formulation was able to elicit a comparable immune response (in terms of IgG and opsonophagocytic activity (OPA) titers) in animals as did the licensed 13vPnC vaccine without the 2-PE preservative.
No dedicated safety pharmacology studies have been conducted with the 13vPnC with 2-PE formulation. However, single-dose studies conducted in rabbits demonstrated no effects on either the central nervous, respiratory, or cardiovascular systems.

Pharmacokinetics:

Pharmacokinetics studies are normally not required for vaccines according to WHO guidelines on nonclinical evaluation of vaccines Annex 1 (TRS, No. 927, 2005).

Toxicology:

Repeat-dose toxicity of the 13vPnC with 2-PE formulation was evaluated in NZW rabbits by the IM route. The candidate vaccine was administered once every 3 weeks for a total of 5 doses at 0.5 mL per dose. The 13vPnC with. 2-PE formulation did not demonstrate evidence of systemic toxicity and was well tolerated, producing only an expected local inflammatory reaction that was reversible, and generated an expected anti-13vPnC antibody response. No new findings were apparent in rabbits administered the 13vPnC with 2-PE formulation compared with what has previously been reported for 13vPnC.

Overall conclusion:

The non-clinical findings confirm that the addition of 2-PE and the use of a multidose vial presentation do not adversely affect the immunogenicity or safety profile of Prevenar 13, and they support the clinical development and use of this formulation, particularly for immunization programs in resource-limited settings.

5. Clinical aspect:

Prevenar 13 (13-valent pneumococcal conjugate vaccine, 13vPnC) is a licensed pneumococcal vaccine approved in the EU since December 2009 and widely used globally, including in Egypt. It contains polysaccharides from 13 pneumococcal serotypes individually conjugated to the carrier protein CRM197. The vaccine is available as a single-dose prefilled syringe (SDS) and as a multidose vial (MDV) formulation containing the preservative 2-phenoxyethanol (2-PE), which has been WHO prequalified for use in developing countries.

Study B4671001 was a Phase III, randomized, open-label trial in healthy infants evaluating the safety, tolerability, and immunogenicity of the 13vPnC MDV formulation compared with the licensed SDS formulation. Vaccines were administered concomitantly with routine pediatric immunizations according to local schedules.

- **Efficacy and Immunogenicity Overview**

The multidose vial formulation of Prevenar 13 demonstrated immunogenicity comparable to the single-dose syringe formulation:

- **Primary endpoint:** ≥95.1% of subjects in both groups achieved pneumococcal IgG concentrations ≥0.35 µg/mL for all 13 serotypes one month after Dose 3.
- **Non-inferiority:** Non-inferiority criteria were met for all 13 serotypes for both IgG response rates and IgG geometric mean concentrations (GMCs).
- **IgG GMCs:** Overall GMCs were similar between formulations, with small, non-clinically concerning differences observed for serotypes 3 and 18C.
- **Functional immunity (OPA):** High proportions of subjects achieved OPA titers ≥LLOQ for most serotypes in both groups, and OPA geometric mean titers were generally comparable between formulations.

These findings confirm that the MDV formulation elicits robust and functional immune responses consistent with the established efficacy profile of Prevenar 13.

- **Safety Overview**

Both vaccine presentations were well tolerated with similar safety profiles:

- **Local reactions:** Low and comparable rates of injection-site tenderness, redness, and swelling; reactions were predominantly mild, short-lived, and resolved within a few days. No severe local reactions were reported.
- **Systemic events:** Common events included irritability, decreased appetite, and increased sleep, with similar frequencies between groups. Fever was infrequent (≤3.6%) and no high-grade fever (≥40°C) occurred.
- **Adverse events:** Overall adverse event rates were similar between groups and were mostly mild in severity.
- **Serious adverse events:** One case of sudden infant death syndrome was reported and was assessed as not related to vaccination. No vaccine-related serious adverse events or new safety signals were identified.

- **Benefit–Risk Conclusion**

The benefit–risk profile of Prevenar 13 remains highly favorable. The MDV formulation provides immunogenicity and safety comparable to the licensed SDS formulation while offering programmatic advantages, including reduced wastage and improved vaccine accessibility in resource-limited settings. Observed differences in immune responses between formulations were small, inconsistent, and not clinically meaningful, and no new safety concerns were identified.

- **Overall Conclusion**

The Phase 3 study confirms that Prevenar 13 formulated in multidose vials with 2-phenoxyethanol is non-inferior to the single-dose syringe formulation in terms of immunogenicity and has a comparable safety and tolerability profile. These findings support the continued use of both presentations of Prevenar 13 for routine infant immunization without raising any concerns regarding efficacy or safety.

For more information, please visit EMA published assessment report link:

https://www.ema.europa.eu/en/documents/variation-report/prevenar-13-h-c-001104-p46-073-epar-assessment-report_en.pdf