Central Drugs Standard Control Organization

Directorate General of Health Services, Ministry of Health and Family Welfare,
Government of India FDA Bhawan, ITO, Kotla Road, New Delhi -110002

Annexure - VIII

SUMMARY OF TECHNICAL EVALUATION REPORT

(PUBLIC ASSESSMENT REPORT)

Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) I.P., 20-Valent

M/s Pfizer Limited, The Capital - A Wing, 1802, 18th Floor, Plot No. C - 70, G Block, Bandra Kurla Complex, Bandra (East), Mumbai, Maharashtra (India)

1. **Generic name:**
   Pneumococcal polysaccharide conjugate vaccine (Adsorbed) I.P., 20-Valent. [PREVENAR-20®]

2. **Description and Dosage Form:**
   The Prevenar-20 vaccine is a sterile liquid suspension for intramuscular administration of capsular polysaccharide antigens of *Streptococcus pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F and 33F with each saccharide individually conjugated to diphtheria cross reactive material (CRM_{197}). Each prefilled syringe of Prevenar-20 vaccine is designed to deliver 2.2 µg of each conjugate serotype (except serotype 6B) and 4.4 µg of conjugate serotype 6B in 0.5 mL dose of vaccine. The vaccine is formulated in 5 mM succinate buffer containing 0.88% sodium chloride (NaCl) and 0.02% polysorbate 80, at pH 5.8, and containing aluminum phosphate at 0.25 mg/mL aluminum as an adjuvant. Each 1 mL syringe contains a 0.5 mL dose of vaccine, supplied as a single-dose injection for parenteral administration, with no preservative.

3. **Presentation approved:**
   Suspension for injection provided in a single-dose (0.5 mL) pre-filled syringe with needle in pack sizes of 1 and 10.

4. **Compositions (components and its quantity per dose)**

Each dose (0.5 mL) of the vaccine contains	
Active ingredients	**Quantity**
Pneumococcal polysaccharide serotype 1[1,2]	2.2µg
Pneumococcal polysaccharide serotype 3[1,2]	2.2µg
Pneumococcal polysaccharide serotype 4[1,2]	2.2µg
Pneumococcal polysaccharide serotype 5[1,2]	2.2µg
Pneumococcal polysaccharide serotype 6A[1,2]	2.2µg
Pneumococcal polysaccharide serotype 6B[1,2]	4.4µg
Pneumococcal polysaccharide serotype 7F[1,2]	2.2µg
Pneumococcal polysaccharide serotype 8[1,2]	2.2µg

Pneumococcal polysaccharide serotype 9V[1,2]	2.2µg
Pneumococcal polysaccharide serotype 10A[1,2]	2.2µg
Pneumococcal polysaccharide serotype 11A[1,2]	2.2µg
Pneumococcal polysaccharide serotype 12F[1,2]	2.2µg
Pneumococcal polysaccharide serotype 14[1,2]	2.2µg
Pneumococcal polysaccharide serotype 15B[1,2]	2.2µg
Pneumococcal polysaccharide serotype 18C[1,2]	2.2µg
Pneumococcal polysaccharide serotype 19A[1,2]	2.2µg
Pneumococcal polysaccharide serotype 19F[1,2]	2.2µg
Pneumococcal polysaccharide serotype 22F[1,2]	2.2µg
Pneumococcal polysaccharide serotype 23F[1,2]	2.2µg
Pneumococcal polysaccharide serotype 33F[1,2]	2.2µg
[1]Conjugated to CRM_{197} carrier protein (approximately 51µg per dose) [2]Adsorbed on aluminium phosphate (0.125 mg aluminium per dose)	
Inactive ingredients	**quantity**
Succinic acid	0.2950 mg
Sodium Chloride	4.4 mg
Polysorbate 80 (PS80)	0.1 mg
Water for Injection	0.5 mL

5. Approved indication of the vaccine:

Active immunisation for the prevention of invasive disease and pneumonia caused by *Streptococcus pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15 B, 18C, 19A, 19F, 22F, 23F, 33F in individuals 18 years of age and older.

Prevenar 20 is not approved in infants, children, and adolescents from 6 weeks to less than 18 years of age in India.

6. Posology of the Vaccine:

For individuals of 18 years of age and older, Prevenar 20 is administered as a single dose. For intramuscular use only – 0.5 mL of Prevenar 20 preferably in the deltoid muscle.

7. Instructions for administration:

One dose (0.5 mL) of Prevenar 20 should be administered intramuscularly, preferably in the deltoid muscle, with care to avoid injection into or near nerves and blood vessels.

For instructions on the handling of the vaccine before administration, Storage and handling instructions are provided in summary of product characteristics.

8. Handling of Multi dose vial:

Not applicable, since Prevenar 20 is approved as single dose pre-filled syringe.

9. Concomitant medication (If any):

Individuals 18 years of age and older- Prevenar 20 may be administered concomitantly with seasonal influenza vaccine (QIV; surface antigen, inactivated, adjuvanted). In subjects with underlying conditions associated with a high risk of developing life-threatening pneumococcal disease, consideration may be given to separating administrations of QIV and Prevenar 20 (e.g., by approximately 4 weeks). In a double-blind, randomised study (B7471004) in adults 65 years of age and older, the immune response was formally non-inferior, however numerically lower titres were observed for all pneumococcal serotypes included in Prevenar 20 when given concomitantly with seasonal influenza vaccine (QIV, surface antigen, inactivated, adjuvanted) compared to when Prevenar 20 was given alone. The clinical relevance of this finding is unknown.

10. Precaution for use:

a) In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.
b) Hypersensitivity - as with all injectable vaccines, appropriate medical treatment and supervision must always be readily available in case of a rare anaphylactic reaction following the administration of the vaccine.
c) Concurrent illness- Vaccination should be postponed in individuals 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.
d) Thrombocytopenia and coagulation disorders - The vaccine must be administered with caution to individuals with thrombocytopenia or a bleeding disorder since bleeding may occur following an intramuscular administration. The risk of bleeding in patients with coagulation disorders needs to be carefully evaluated before intramuscular administration of any vaccine, and subcutaneous administration should be considered if the potential benefit clearly outweighs the risks.
e) Protection against pneumococcal disease - Prevenar 20 may only protect against *Streptococcus pneumoniae* serotypes included in the vaccine, and will not protect against other microorganisms that cause invasive disease, pneumonia or otitis media (OM). As with any vaccine, Prevenar 20 may not protect all individuals receiving the vaccine from invasive pneumococcal disease (IPD), pneumonia or OM.
f) Immunocompromised individuals - Safety and immunogenicity data on Prevenar 20 are not available for individuals in immunocompromised groups. Vaccination should be considered on an individual basis.

11. Storage conditions:

Store in a refrigerator (2°C to 8°C). Pre-filled syringes should be stored in the refrigerator horizontally to minimise the resuspension time. Do not freeze. Discard if the vaccine has been frozen.

12. Shelf Life approved:

The shelf life of 20vPnC drug product is 24 months when stored at the recommended temperature of 2-8° C.

13. Precaution for storage (If any):

- Store in a refrigerator (2 ℃ to 8 C). Pre-filled syringes should be stored in the refrigerator horizontally to minimise the resuspension time.
- Do not freeze. Discard if the vaccine has been frozen.
- From a microbiological point of view, once removed from the refrigerator, the vaccine should be used immediately.
- Stability data indicate that the vaccine is stable for 96 hours when stored at temperatures from 8° C to 25° C or 72 hours when stored at temperatures from 0° C to 2° C. At the end of these time periods Prevenar 20 should be used or discarded. These data are intended to guide healthcare professionals in case of temporary temperature excursion only.

14. Brief Description on container closure of drug product

Pre-filled syringes (PFS) (Type I borosilicate glass) with a tip cap (synthetic isoprene/bromobutyl blend rubber) and a plunger stopper (chlorobutyl rubber).

15. Regulatory status in India and other Countries:

Pneumococcal Polysaccharide conjugate vaccine (Adsorbed) I.P., 20-Valent Prevenar 20) in PFS has been approved in more than 52 countries including United States and European Union and currently marketed in more than 35 countries.

16. The country of origin of imported product, responsible NRA and address (not applicable for indigenous vaccine):

European Medicine Agency, Domenico Scarlattilaan 6, 1083 HS Amsterdam, the Netherlands.

17. Brief summary and conclusion of safety & Immunogenicity/efficacy of Phase I, II and III clinical trials separately:

a) Phase I Studies in United States: -

- Phase 1 First-in-human randomized, active-controlled, observer-blinded trial (B7471001) was conducted at one site in US to evaluate safety and immunogenicity of 20vPnC in healthy pneumococcal vaccine naïve adults 18 through 49 years of age. A tetanus, diphtheria and acellular pertussis vaccine (Tdap) control was chosen to benchmark the safety and tolerability of 20vPnC to a vaccine licensed and recommended for use in this population. There were no safety issues identified in this Phase 1 study. The immunogenicity data from this study demonstrate that the

administration of 20vPnC was well tolerated and induced functional (OPA) and IgG immune responses to all vaccine serotypes.

- Phase 1b, randomized, controlled, double-blind study of the safety and immunogenicity of 20vPnC and c7vPnC was conducted in Japanese adults residing in the US. The study had a 3-arm parallel design planned in approximately 99 healthy adults 18 through 49 years of age with no history of pneumococcal vaccination. Participants were enrolled and randomized equally to receive a single dose of 20vPnC, c7vPnC, or 13vPnC (control group). Based on the study results it is concluded that the administration of 20vPnC and c7vPnC was well tolerated, and few AEs were reported. The data also demonstrate that 20vPnC and c7vPnC induce specific functional OPA immune responses that are anticipated to be associated with protection. Overall, these results support continued development of 20vPnC and c7vPnC in Japan.

b) Phase II study in United States: -

Phase 2, multicentre, randomized, active-controlled, double-blind trial (B7471002) with a 2-arm parallel design either: a single dose of 20vPnC (Vaccination 1) followed 1 month later by saline placebo (Vaccination 2) administration in the 20vPnC/saline group, or a single dose of 13vPnC (Vaccination 1) followed 1 month later by a dose of PPSV23 (Vaccination 2) in the 13vPnC/PPSV23 group (control group) was conducted across 14 sites to evaluate the safety and immunogenicity of 20vPnC in total 440 adults aged 60 to 64 years with no history of pneumococcal vaccination. Adults in this age group are at higher risk for pneumococcal disease compared with younger adults, and are also more likely to be pneumococcal vaccine naïve compared with adults ≥65 years of age. Based on the study results it is observed that the administration of 20vPnC was well tolerated, and AEs reported in the study were consistent with medical events or conditions that are common to this age group. The safety profile was similar to 13vPnC, and there were no safety signals identified in this Phase 2 study. The data also demonstrate that the 20vPnC induces functional OPA immune responses that are anticipated to be associated with protection. Overall, these results support continued development of the 20vPnC program.

c) Phase III studies in countries other than India:

- Phase 3 randomized, open-label trial (B7471006) was conducted in adults ≥65 years of age with prior Pneumococcal vaccination with sample size of 875 individuals at 33 sites in US and 8 sites in Sweden. Study design consists of 3 different cohorts based on their prior pneumococcal vaccination history. The study shows that the safety and tolerability profile of 20vPnC was generally similar in participants with different prior pneumococcal vaccine history and was generally similar to 13vPnC and PPSV23 control groups. 20vPnC elicits immune responses to all 20 vaccine serotypes in adults 65 years of age and above in individuals who have previously received pneumococcal vaccine,

with the strongest responses noted in persons who have previously received 13vPnC only.

- Pivotal Phase 3 randomized, active-controlled, double-blind noninferiority trial (B7471007) was conducted in approximately 3880 pneumococcal vaccine naïve adults ≥ 18 years of age at 54 sites in the US and 7 sites in Sweden. 20vPnC was observed to have a tolerability and safety profile similar to 13vPnC. Based on the robust immune responses and comparability to licensed pneumococcal vaccines (13vPnC and PPSV23) for applicable serotypes, as well as bridging to the younger age groups, these data support that 20vPnC will be protective against pneumococcal disease due to the 20 serotypes in adults.

- Phase 3 randomized, double-blind lot consistency trial (B7471008) was conducted across 21 sites in the US. to evaluate the immunogenic equivalence of 3 separately manufactured lots of 20vPnC in approximately 1610 adults 18 through 49 years of age with no history of pneumococcal vaccination. A 13vPnC control group was included for safety assessment only. Participants were randomized into 1 of 4 groups in a 2:2:2:1 ratio (20vPnC Lot 1: 20vPnC Lot 2: 20vPnC Lot 3: 13vPnC) by site-based randomization. This study shows that equivalence in immune responses was demonstrated across 3 lots of 20vPnC, and robust responses were elicited to the 20 vaccine serotypes. Safety profiles across 3 lots of 20vPnC were similar, and the overall safety and tolerability profile of 20vPnC was acceptable and similar to 13vPnC.

Each above said phase 3 study included participants who were healthy or immunocompetent with stable underlying conditions, including chronic cardiovascular disease, chronic pulmonary disease, renal disorders, diabetes mellitus, chronic liver disease, and medical risk conditions and behaviours (e.g., smoking) that are known to increase the risk of serious pneumococcal pneumonia and IPD. In the pivotal study (Study 1007), these risk factors were identified in 34%, 32%, and 26% of participants 60 years of age and over, 50 to 59 years of age, and 18 to 49 years of age, respectively. A stable medical condition was defined as a medical condition not requiring significant change in therapy in the previous 6 weeks (i.e., change to new therapy category due to worsening disease), or any hospitalization for worsening disease within 12 weeks before receiving the study vaccine.

In each study, immune responses elicited by Prevenar 20 and the control pneumococcal vaccines were measured by an opsonophagocytic activity (OPA) assay. OPA assays measure functional antibodies to *S. pneumoniae.*

d) Phase III study in India

Phase 3 single-arm, multicenter study (B7471010) was conducted to assess the safety and immunogenicity of 20vPnC in adults ≥18 years of age in India. 400 eligible participants were assigned into 2 cohorts by age (200 participants per cohort): 18 to 49 years of age and ≥50 years of age.

Safety results: A total of 400 participants received a single dose of Prevenar 20 and were included in the safety population. The percentage of participants reporting any AEs from vaccination to 1 month after vaccination was low, 2.3% in the overall population, and 1.5% and 3.0% respectively in the 18-49 years of age cohort and ≥50 years of age cohort. Most local reactions and systemic events were mild or moderate in severity. No safety concerns were identified. No AEs were considered related to Prevenar 20 in this study. No immediate AEs, severe AEs, deaths, or SAEs were reported in this study.

Immunogenicity results: Immune responses to all 20 vaccine serotypes 01 month after vaccination with Prevenar 20 were observed in adults 18-49 and ≥50 years of age, based on serotype specific OPA GMFR, OPA GMTs, percentages of participants with a ≥4-fold-rise in OPA titers, and percentages of participants with OPA titers ≥ lower limit of quantitation (LLOQ).

Conclusion:

20vPnC was observed to be well tolerated with an acceptable safety profile in Indian adults ≥18 years of age. Immune responses data following 1 dose of 20vPnC supports that 20vPnC is expected to provide protection against pneumococcal disease due to the 20 serotypes in adults ≥18 years of age in India.

18. Brief summary of review process of dossier (CTD format, CMC, CDL, SEC, GMP conclusions etc.):

The firm has submitted New Drugs application through SUGAM online portal system in CTD format (Module-I, II, III, IV & V) for grant of import permission under New Drugs & Clinical Trial Rules, 2019 for Pneumococcal polysaccharide conjugate vaccine (Adsorbed) I.P., 20-Valent in) in pre-filled syringe (Type I borosilicate glass) with a tip cap (synthetic isoprene/bromobutyl blend rubber) and a plunger stopper (chlorobutyl rubber) containing 0.5 mL dose of vaccine, supplied as a single-dose injection for parenteral administration, with no preservative from M/s Pfizer Limited., Pfizer Manufacturing Belgium NV, Rijksweg 12, Puurs- Sint-Amands,2870, Belgium.

In view of above and based on the submission of documents/information & review of the CMC data which includes manufacturing, testing, process validation & stability data of drug substance and drug product, non-clinical data, Phase I, Phase-II & Phase-III CT report of US & Sweden and Phase III clinical trial in Indian subjects along with the recommendations of SEC-Vaccine meeting dated 26.11.2024, recommendation of CDL, Kasauli on dossiers and two batches test

reports from CDL, Kasauli, the benefit-risk evaluation of study vaccine, Prevenar-20 was considered favourable for grant of permission in Form CT-20 to import Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) I.P., 20-Valent, (PREVENAR-20) from M/s Pfizer Manufacturing Belgium NV, Rijksweg 12, 2870 Puurs-Sint-Amands Belgium to Marketing Authorization holder in India, M/s. Pfizer Limited, The Capital-A Wing, 1802, 18th Floor, Plot No. C-70, G Block, Bandra Kurla Complex, Bandra (East), Mumbai, Maharashtra-400051, India in single-dose (0.5 mL) pre filled syringe (Type I borosilicate glass) with needle in pack sizes of 1 and 10 for intramuscular administration with the shelf life of 24 months stored at 2°C to 8°C for sale or for distribution for "Active immunisation for the prevention of invasive disease and pneumonia caused by Streptococcus pneumoniae serotypes 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F, 33F in individuals 18 years of age and older".