6.4. Special precautions for Storage
Store at +2°C to +8°C. DO NOT FREEZE. Discard if found frozen. Shake vigorously before use. Keep out of reach of children.

Handling of multidose vial once opened:
Once opened, multi-dose vials should be kept between +2°C and +8°C. Multi-dose vials of Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (14-valent) from which one or more doses of vaccine have been removed during an immunization session may be used in subsequent immunization sessions for up to a maximum of 28 days, provided that all of the following conditions are met:

- The vaccine is approved for use for up to 28 days after opening the vial
- The expiry date has not passed
- The vaccine vial has been, and will continue to be, stored at manufacturer recommended temperatures; furthermore, the vaccine vial monitor if one is attached, is visible on the vaccine label and is not past its discard point, and the vaccine has not been damaged by freezing.

6.5. Nature and contents of container
BE-PCV14 is filled in USP type I glass vials and closed using bromobutyl rubber stoppers and sealed with aluminium flip-off seals.
The vaccine is filled in to single dose and five dose presentations and is offered in the following presentations:

- Single dose Vial of 0.5 mL
- Multi dose Vial of 2.5 mL

The above presentations are offered in different packaging configuration as per the requirement. Not all pack sizes may be marketed.

6.6. Special precautions for disposal
Any unused product or waste material should be disposed of in accordance with local requirements

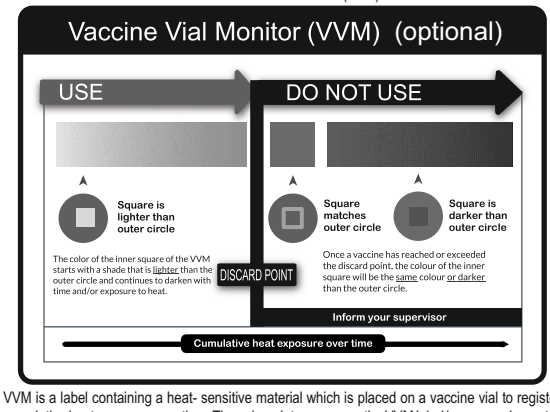
6.7. Patient Counselling Information
BE-PCV14 is a conjugate vaccine containing polysaccharides from serotypes 1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F, and 33F conjugated to non-toxic diphtheria toxin cross-reacting material (CRM_{197}) The body is expected to develop an immune response against the injected 197 serotypes which would help in prevention of disease caused by Streptococcus pneumoniae. Most common adverse events that have been reported with the BE-PCV14 are injection site pain or tenderness. Other common systemic adverse events reported are fever and injection site redness. There is a remote chance that BE-PCV14 could cause a severe allergic reaction. A severe allergic reaction may very rarely occur after getting a dose of BE-PCV14. For this reason, your vaccination provider will ask you to stay for 30 minutes after each dose of vaccination at the place where you received your vaccine for monitoring after vaccination.
Signs of a severe allergic reaction can include:

- Difficulty in breathing
- Swelling of your face and throat
- A fast heart beat
- Rash all over your body
- Dizziness and weakness

If the vaccinee experiences any of the above side effect(s), please contact or visit your health care provider / vaccinator / officer supervising your vaccination or immediately go to the nearest hospital.

7. Instructions for use, handling and disposal
Each vaccine dose of 0.5 mL is withdrawn into a syringe for injection to be administered intramuscularly. Use a separate sterile needle and syringe for each individual.

7.1. Vaccine Vial Monitoring (VVM)
The Vaccine is available with or without Vaccine Vial Monitor (VVM).



VVM is a label containing a heat- sensitive material which is placed on a vaccine vial to register cumulative heat exposure over time. The colour dot appears on the VVM label in square element is a time - temperature sensitive dot that provides an indication of the cumulative heat to which the vial has been exposed. It warns the end user when exposure to heat is likely to have degraded the vaccine beyond an acceptable level.
The interpretation of the VVM is simple. Focus on the central square. Its colour will change progressively. As long as the colour of this square is lighter than the colour of the ring, then the vaccine can be used. As soon as the colour of the central square is the same colour as the ring or of a darker colour than the ring, then the vial should be discarded.

8. Details of manufacturer

BE *Biological E. Limited*

Registered office:
18/1 & 3, Azamabad, Hyderabad, Telangana - 500 020, INDIA.

Manufacturing Site Address:
Plot No. 1, Biotech Park, Phase II, Kolthur Village, Shameerpet,
Medchal-Malkajgiri District, Telangana, India - 500 078.
Web site: www.biologicale.com
®- Registered Trade Mark

9. Details of permission or licence number with date
Permission No: MF/BI0/22/000112
Date of issue: 10-Dec-2022

10. Date of revision
Oct 2025

You can help by reporting any side effects that you may get after vaccination to Biological E. Limited (BE), who is the manufacturer of **PNEUBEVAX 14®** on:
E-mail at pharmacovigilance@biologicale.com
For adverse event reporting online: https://www.biologicale.com
For more information, read this Package Insert carefully.

6xxx.01 ENG

Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (14 Valent)

PNEUBEVAX 14®

1. Name of the Medicinal Product
Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (14-valent)

2. Composition
Single Dose (0.5 mL) Presentation:
Each dose of 0.5 mL contains:
Single Dose (0.5 mL) Presentation:
Each dose of 0.5 mL contains:

Pneumococcal polysaccharide serotype 1	3.0 µg
Pneumococcal polysaccharide serotypes 3, 4, 5, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F and 33F (each)	2.2 µg
Pneumococcal polysaccharide serotype 6B	4.4 µg
Adsorbed onto Aluminium Phosphate, as Al^{+++}	≤ 0.75 mg
Polysaccharides conjugated to 20-50 µg of CRM_{197}	

Multi Dose (2.5 mL) Presentation:
Each dose of 0.5 mL contains:

Pneumococcal polysaccharide serotype 1	3.0 µg
Pneumococcal polysaccharide serotypes 3, 4, 5, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F and 33F (each)	2.2 µg
Pneumococcal polysaccharide serotype 6B	4.4 µg
Adsorbed onto Aluminium Phosphate, as Al^{+++}	≤ 0.75 mg
2- Phenoxyethanol	4 mg
Polysaccharides conjugated to 20-50 µg of CRM_{197}	

3. Pharmaceutical Form
BE-PCV14 is a whitish suspension in which the mineral carriers tend to settle down slowly. The vaccine contains *Streptococcus pneumoniae* serotypes 1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F and 33F. These polysaccharides are conjugated using CRM_{197}. The antigens are adsorbed onto Aluminium Phosphate as an adjuvant. 2-Phenoxyethanol is used as preservative only in multi-dose presentation.

4. Clinical Particulars
4.1. Therapeutic Indications
BE-PCV14 is indicated for active immunization against invasive diseases, pneumonia and otitis media caused by *Streptococcus pneumoniae* serotypes 1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F, 33F and cross reactive 6A, in children from 6 weeks of age.

4.2. Posology and Method of Administration
BE-PCV14 is to be administered as a three dose primary series in infants at 6-10-14 weeks or a two dose primary series at 6 weeks-14 weeks with a booster at 9 months.
The vaccine should be administered intramuscularly. The preferred site is anterolateral aspect of the upper thigh. The vaccine should not be injected in the gluteal area. Use a separate sterile needle and syringe for each individual. The vaccine should not be injected intradermally, subcutaneously or intravenously, since the safety and immunogenicity of these routes have not been evaluated.

Vaccination schedule for infants				
Dosage schedule	6 weeks	10 weeks	14 weeks	9 months*
3p+0	Dose 1	Dose 2	Dose 3	–
2p+1	Dose 1	–	Dose 2	Dose 3

Dose 1 can be given as early as 6 weeks of age
The recommended dosing interval for primary series is 4 to 8 weeks
*Booster dose is recommended at 9 months of age
p:primary dose

For children who are beyond the age of routine infant schedule, the National Recommendation should be followed.
The vaccine vial should be shaken vigorously to obtain a uniform suspension before use. Prior to administration, the vaccine vial should be visually checked for complete suspension and/or presence of any particulate matter. In the event of either being observed, discard the vaccine. Sterile needle and syringe should be used for withdrawal of the vaccine.

4.3. Contraindications
Hypersensitivity to any constituents of the vaccine listed in section 6.1

4.4. Special Warnings and Precautions for Use

- Do not administer intravenously, intradermally, or subcutaneously.
- Like all other vaccines, supervision and appropriate medical treatment should always be available to treat any anaphylactic reactions following immunization
- **The vaccinee should remain under medical supervision for at least 30 minutes after vaccination**
- **Concurrent illness**: As with other vaccines, administration of BE-PCV14 should be postponed in individuals suffering from an acute severe febrile illness.
- Adrenaline Injection (1:1000) should be available in case of acute Anaphylactic reaction following vaccination.
- **Thrombocytopenia and coagulation disorders**: As with any other intramuscular injection, BE-PCV14 should be given with caution in individuals with thrombocytopenia and coagulation disorders or to individuals on treatment with anticoagulation therapy, because of risk of bleeding or bruising following an intramuscular injection in these individuals.
- **Immunocompromised individuals**: it is not known if individuals with impaired immune responsiveness, including individuals receiving immunosuppressant therapy, will elicit the same response as immunocompetent individuals to BE-PCV14. These individuals may have a weaker immune response to the vaccine.

SPECIAL POPULATIONS:
Currently, safety and immunogenicity data for the BE's 14-valent Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) are not available for children belonging to specific high-risk groups for invasive pneumococcal disease—such as those with congenital or acquired splenic dysfunction, HIV infection, malignancies, or nephrotic syndrome. These children may exhibit a diminished antibody response to active immunization due to compromised immune function. Although limited, existing data on other pneumococcal conjugate vaccines suggest that they can elicit an immune response in children with HIV, sickle cell disease, and in premature infants, with safety profiles comparable to those seen in children not considered high risk. Use of the BE's 14-valent Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) in high-risk pediatric groups should be evaluated on a case-by-case basis, taking individual clinical circumstances into account.
Premature Infants: Experience with other pneumococcal conjugate vaccines suggests a potential risk of apnoea following vaccination in very premature infants (born at ≤28 weeks gestation), particularly in those with a history of respiratory immaturity. Therefore, consideration should be given to monitoring respiratory function for 48 to 72 hours after administration of the primary immunization series in this population. BE-PCV14 has not been studied in premature infants in the clinical trials. As the benefit of vaccination is high in this group of infants, vaccination with Pneumococcal Polysaccharide conjugate vaccine (Adsorbed) (14-valent) should not be withheld or delayed.

4.5. Drugs interactions
BE-PCV14 can be given with either monovalent or combination vaccines containing diphtheria, tetanus, whole-cell pertussis, hepatitis B, *Haemophilus influenzae* type b, inactivated or oral poliomyelitis and Rotavirus vaccine. Clinical studies demonstrated that the safety and immunogenicity profiles of the administered vaccines were unaffected. For concomitant administration, use different injection sites and separate syringes.

4.6. Use in special populations (such as pregnant women, lactating women)
Safety and effectiveness have not been established in pregnant women, nursing mothers. It is not known whether the vaccine is excreted in human milk.

4.7. Effect on ability to drive and use machines

No studies on the effect of BE-PCV14 on the ability to drive and use machines have been performed.

4.8. Undesirable effects

Clinical Trial Experience: The safety of BE's Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) I.P. (14 Valent) [BE-PCV14] was established in 6-8-week-old infants in 6-10-14 weeks primary schedule, 6 weeks-14 weeks and 9 months schedule,12-23 months old toddlers and 18-45-year-old adult individuals. Within each system organ class (SOC) the adverse reactions were ranked under headings using the following convention:

Expected frequency of adverse events in vaccinees

Very common	≥ 10%
Common	≥ 1% and < 10%
Uncommon	≥ 0.1% and < 1%
Rare	≥ 0.01% and < 0.1%
Very rare	≤ 0.01%

Systemic:

Common (≥ 1% and < 10%)
- Fever/Pyrexia
- Irritability Postvaccinal
- Diarrhoea

Uncommon (≥ 0.1% and < 1%)
- Chills
- Crying
- Decreased appetite
- Somnolence
- Vomiting

Local:

Very common (≥ 10%)
- Injection site pain (tenderness)

Common (≥ 1% and < 10%)
- Injection site erythema
- Injection site induration/swelling

Summary of safety profile:

In the Phase I study (BECT043), conducted in 24 healthy adult subjects aged 18 to 45 years, the most commonly reported local adverse events were injection site pain, erythema, and tenderness. All local reactions were assessed as related to the study vaccine. The most frequently reported systemic adverse events included chills, headache, fever (pyrexia), and rash. According to the principal investigator, all systemic adverse events were considered vaccine-related.

In the Phase II study (BECT044), 120 healthy, pneumococcal vaccine-naïve Indian toddlers aged 12 to 23 months were enrolled and randomized in a 1:1 ratio to receive either BE-PCV14 or a licensed 13-valent pneumococcal conjugate vaccine as a comparator. In the BE-PCV14 group, the most frequently reported treatment-emergent adverse events (by preferred term) included injection site pain, pyrexia, injection site swelling, erythema/redness at the injection site, crying, and decreased appetite.

In the controlled Phase-III (BECT051) study conducted in 1290 infants of 6-8 weeks old in 6-10-14 weeks dosing schedule, randomized in 1:1 ratio between BE-PCV14 or 13 valent licensed comparator, the safety profile of BE-PCV14 was comparable to the licensed PCV in terms of overall AE rates, related AE rates and medically attended AEs. The total number of subjects with at least one adverse event reported in BE-PCV14 group were 175/645 (27.1%) as against 178/645 (27.6%) in the licensed comparator group. The number of subjects reporting at least one adverse event were similar in BE-PCV14 and licensed comparator groups. Out of total 1290 enrolled subjects, 175/645 (27.1%) subjects reported 355 events and 178/645 (27.6%) subjects reported 353 events in BE-PCV14 and licensed comparator groups respectively. The most frequently reported adverse events in BE-PCV14 group were Injection site pain [133 AEs in 93 (14.4%) subjects], Pyrexia [53 AEs in 42 (6.5%) subjects], Injection site swelling [51 AEs in 44 (6.8%) subjects], Injection site erythema [38 AEs in 33 (5.1%) subjects], Irritability postvaccinal [41 AEs in 25 (3.9%) subjects], Injection site induration [13 AEs in 9 (1.4%) subjects], Decreased appetite [9 AEs in 8 (1.2%) subjects], Diarrhoea [8 AEs in 6 (0.9%) subjects], Vomiting [3 AEs in 3 (0.5%) subjects] and Somnolence [4 AEs in 2 (0.3%) subjects]. The most frequently reported adverse events in licensed comparator group were Injection site pain [131 AEs in 98 (15.2%) subjects], Pyrexia [51 AEs in 40 (6.2%) subjects], Injection site swelling [58 AEs in 48 (7.4%) subjects], Injection site erythema [44 AEs in 36 (5.6%) subjects], Irritability postvaccinal [31 AEs in 21 (3.3%) subjects], Injection site induration [18 AEs in 13 (2.0%) subjects], Decreased appetite [10 AEs in 6 (0.9%) subjects], Vomiting [5 AEs in 4 (0.6%) subjects], Diarrhoea [3 AEs in 2 (0.3%) subjects] and Somnolence [2 AEs in 1 (0.2%) subjects].

In another controlled Phase-III (BECT061) study conducted in 300 infants of 6-8 weeks old in 6-10-14 weeks dosing schedule, randomized in 1:1 ratio between BE-PCV14 or 13-valent licensed comparator, the safety profile of BE-PCV14 was comparable to the control vaccine licensed comparator in terms of overall AE rates, related AE rates and medically attended AEs. The most frequently reported adverse events in BE-PCV14 group were Injection site pain [24 AEs in 17 (11.3%) subjects], Injection site swelling [14 AEs in 10 (6.7%) subjects], Injection site erythema [10 AEs in 10 (6.7%) subjects], Irritability postvaccinal [12 AEs in 5 (3.3%) subjects], Pyrexia [5 AEs in 5 (3.3%) subjects] and Injection site induration [1 AE in 1 (0.7%) subject]. The most frequently reported adverse events in licensed comparator group were Injection site pain [25 AEs in 19 (12.7%) subjects], Injection site swelling [16 AEs in 13 (8.7%) subjects], Pyrexia [13 AEs in 12 (8.0%) subjects], Irritability postvaccinal [9 AEs in 6 (4.0%) subjects], Injection site erythema [7 AEs in 7 (4.7%) subjects] and Vomiting [1 AE in 1 (0.7%) subject].

Across both Phase III studies, all reported adverse events were of mild to moderate intensity. The majority of AEs were assessed by investigators as related to the study vaccine and were solicited in nature. No severe adverse events, serious adverse events (SAEs), or deaths were reported in either treatment group. There were no clinically meaningful changes observed in vital signs or physical examination findings over time, and no safety concerns were identified based on AE profiles.

In a Phase-III (BECT056) study conducted in 400 infants of 6-8 weeks old in 6weeks, 14 weeks and 9 months (2p+1) dosing schedule, randomized in 1:1 ratio between BE-PCV14 or 13-valent licensed comparator, the safety profile of BE-PCV14 was comparable to the control vaccine licensed comparator in terms of overall AE rates, related AE rates and medically attended AEs. The most frequently reported adverse events in Biological E's 14-valent pneumococcal polysaccharide conjugate vaccine group were Injection site pain [34 (17.50%) subjects with 38 events], Pyrexia [28 (14.00%) subjects with 31 events], Injection site swelling [12 (6.00%) subjects with 12 events] and Injection site erythema [11 (5.50%) subjects with 12 events], Injection site induration [7 (3.50%) subjects with 7 events], Irritability postvaccinal [4 (2.50%) subjects with 4 events], Vomiting [2 (1.00%) subjects with 2 events], Diarrhoea [1 (0.50%) subject with 1 event] and Somnolence [1 (0.50%) subject with 1 event]. The reported AEs were predominantly mild to moderate in severity, and no safety concerns were identified. The results further support the favourable safety profile of BE-PCV14 when administered in a 2p+1 dosing schedule.

In a post marketing, Phase IV study (BECT081) conducted to evaluate the safety of BE- PCV14 administered in a 6-10-14-week dosing schedule to healthy Indian infants aged 6–8 weeks, 26.30% of the 2300 infants who received BE-PCV14 reported adverse events compared to 24.67% of the 300 infants who received licensed comparator vaccine during study period dose 1 to one month after dose 3 (i.e day 84).

The most commonly reported adverse events in BE-PCV14 arm were Pyrexia (14.04% recipients), Injection site pai (10.96% recipients), Injection site swelling (6.35% recipients), Injection site erythema (4.52% recipients), Irritability postvaccinal (2.96% recipients), Injection site Induration (1.78% recipients), Decreased appetite (0.96% recipients) and Diarrhoea (0.96% recipients). In licensed comparator arm, the most commonly reported adverse events were Pyrexia (10.33% recipients), Injection site pain (8.67% recipients), Injection site erythema (5.00% recipients) and Injection site swelling (4.00% recipients).

Adverse Events Reported from day 84 to 6-Month Follow-up Visit:

During the 6-month follow-up period, 1.78% of the participants in the BE-PCV14 arm and 1.00% in the licensed comparator arm reported adverse events. The most commonly reported adverse events in the BE's PCV14 arm were pyrexia (0.78% recipients), vomiting (0.35% recipients), nasopharyngitis (0.26% recipients), and diarrhoea 0.13% (recipients). In the licensed comparator arm, the most commonly reported adverse events were pyrexia (0.67% recipients) and cough (0.33% recipients)

Majority of the reported adverse events were mild in intensity and considered related to the study vaccine. The nature and pattern of adverse events observed were consistent with the known safety profile of other licensed pneumococcal conjugate vaccines.

4.9. Overdose

No case of overdose has been reported. There is no specific treatment for an overdose with BE-PCV14. In the event of an overdose, the individual should be monitored and provided with symptomatic treatment as appropriate.

5. Pharmacological Properties

5.1. Pharmacodynamic Properties

Mechanism of Action

Streptococcus pneumoniae causes paediatric invasive bacterial disease (including bacteraemia, bacterial pneumonia and meningitis), and non-invasive disease (pneumonia and acute otitis media) and is estimated to account for approximately 1 million deaths per year worldwide among children younger than 5 years of age.

Unconjugated bacterial polysaccharides stimulate B cells through a T cell-independent mechanism, resulting primarily in the production of IgM antibodies, which are short-lived. Generally, there is no affinity maturation of the antibodies, and no memory cells are produced, leading to the absence of a booster response to subsequent doses of the same antigen. Conjugation of bacterial polysaccharides to a protein (such as CRM_{197}) results in a T cell-dependent immune response, in which CD4+ T-helper cells activate B cells to proliferate and differentiate into plasma cells. These plasma cells produce IgG antibodies and memory B cells. Affinity maturation leads to the production of high-affinity IgG antibodies, while the presence of memory B cells enables rapid mobilization and antibody secretion upon re-exposure to the same antigen (booster response). Unlike polysaccharide vaccines, which have poor or no immunogenicity in infants and toddlers under 2 years of age, conjugate vaccines are immunogenic across all age groups, including infants and toddlers younger than 24 months. Conjugating *Streptococcus pneumoniae* polysaccharides to the CRM_{197} protein enhances the antibody response, induces long-lasting immune memory, and elicits a booster response upon re-exposure to the same polysaccharide antigen in infants and young children.

BE-PCV14 contains polysaccharides from serotypes 1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F and 33F conjugated to non-toxic diphtheria toxin cross-reacting material (CRM_{197}) providing broader coverage. Serotypes 22F and 33F are added in the BE-PCV14 since these serotypes have emerged as important causes of invasive pneumococcal disease (IPD), particularly in the post-PCV13 era, due to serotype replacement. These serotypes are now among the leading causes of IPD in several regions, especially in infants, older adults, and immunocompromised individuals. Including 22F and 33F in pneumococcal conjugate vaccines broadens protection against strains not covered by earlier-generation vaccines, helping to address the evolving epidemiology of pneumococcal disease and reduce residual disease burden. Their inclusion is supported by surveillance data and aligns with public health goals to enhance effectiveness of pneumococcal conjugate vaccines.

The body develops an immune response against the injected serotypes which would help in prevention of disease caused by *Streptococcus pneumoniae.*

In the clinical trials conducted in healthy infants and toddlers, the vaccine was found to be safe and immunogenic.

Efficacy and Immunogenicity data

In the Phase-II (BECT044) comparative study conducted in 120 subjects aged 12-23 months, randomized in 1:1 ratio between BE-PCV14 or 13 valent licensed comparator given as 2 doses with 2 months apart, the proportion of subjects seroconverted one month after two doses were 96.55% (56), 98.28% (57), 100% (58), 100% (58), 93.10% (54), 100% (58), 100% (58), 100% (58), 100% (58), 98.28% (57), 100% (58), 98.28% (57), 100% (58) and 91.38% (53) against serotypes 1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F and 33F respectively. The immunogenicity of BE-PCV14 was found to be comparable to that of the licensed 13-valent comparator across all shared serotypes and demonstrated robust responses to the additional serotypes 22F and 33F.

In the Phase-III (BECT051) study conducted in 1290 infants of 6-8 weeks old in 6-10-14 weeks dosing schedule, randomized in 1:1 ratio between BE-PCV14 or 13-valent licensed comparator, the proportion of subjects seroconverted at visit 3 (Day 86) were 90.6% (581), 83.5% (535), 93.1% (597), 90.6% (581), 76.3% (489), 95.8% (614), 95.2% (610), 99.7% (639), 90.5% (580), 99.4% (637), 97.2% (623), 94.1% (603), 82.4% (528) and 73.2% (469) against serotypes 1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F & 33F respectively. BE-PCV14 demonstrated immunogenic non-inferiority to licensed 13 valent PCV w.r.t seroconversion rate and Geometric mean concentration ratio for all shared serotypes. The vaccine also induced robust OPA antibodies which were comparable to licensed comparator vaccine.

In another Phase-III (BECT061) study conducted in 300 infants of 6-8 weeks old in 6-10-14 weeks dosing schedule, randomized in 1:1 ratio between BE-PCV14 or 13-valent licensed comparator, the proportion of subjects seroconverted at visit 3 (Day 86) were 93.3% (139), 76.5% (114), 91.3% (136), 88.6% (132), 81.2% (121), 96.6% (144), 94.6% (141), 100.0% (149), 91.3% (136), 100.0% (149), 97.3% (145), 88.6% (132), 86.6% (129) and 67.1% (100) against serotypes 1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F & 33F respectively.

The immune response to serotype 6A was achieved through cross protection from serotype 6B with BE-PCV14, which is evident from two phase III clinical studies.

In Phase III (BECT056) study conducted in 400 infants of 6-8 weeks old in 6weeks, 14weeks and 9 months (2p+1) dosing schedule, randomized in 1:1 ratio between BE-PCV14 or 13-valent licensed comparator, the proportion of subjects seroconverted at Day 84 were Serotype 1 (98.4 %), Serotype 3 (72.6%), Serotype 4 (94.6%), Serotype 5 (94.6%), Serotype 6A (70.4%), Serotype 6B (85.5%), Serotype 7F (97.8%), Serotype 9V (96.8%), Serotype 14 (100%), Serotype 18C (88.7%), Serotype 19A (99.5%), Serotype 19F (100%), Serotype 23F (89.2%), Serotype 22F (95.2%), Serotype 33F (81.2%%).

Day 270 (pre-booster) Serotype 1 (84.9%), Serotype 3 (57%), Serotype 4 (67.7%), Serotype 5 (66.1%), Serotype 6A (69.3%), Serotype 6B (90.9%), Serotype 7F (79.6%), Serotype 9V (69.9%), Serotype 14 (100%), Serotype 18C (55.9%), Serotype 19A (96.2%), Serotype 19F (99.5%), Serotype 23F (70.4%), Serotype 22F (98.9%), Serotype 33F (85.5%).

Day 300 (post-booster) Serotype 1 (97.8%), Serotype 3 (87.6%), Serotype 4 (92.5%), Serotype 5 (91.9%), Serotype 6A (93.0%), Serotype 6B (97.3%), Serotype 7F (95.7%), Serotype 9V (94.6%), Serotype 14 (100%), Serotype 18C (89.2%), Serotype 19A (98.9%), Serotype 19F (99.5%), Serotype 23F (93.5%), Serotype 22F (96.8%), Serotype 33F (92.5%).

BE-PCV14 demonstrated comparable immune response to licensed 13 valent comparator vaccine in 2p+1 schedule for all shared serotypes. Immune response to serotypes 22F, 33F and 6A was also demonstrated. Both vaccines demonstrated good persistence of antibody responses at day 270 (pre-booster) and robust booster responses at day 300 (30 days post booster), indicating successful priming and development of immunological memory.

BE-PCV14 has shown comparable seroconversion rates and serotype specific anti-PnCPS IgG antibody concentrations for the common serotypes of the 13 valent licensed comparator in all the studies conducted so far.

5.2. Pharmacokinetic Properties

Evaluation of pharmacokinetic properties is not required for vaccines.

5.3. Preclinical safety data

Animal Toxicology or Pharmacology:

Single dose toxicity studies in Rats and repeat dose toxicity studies in Rats and Rabbits were conducted. Based on the toxicity studies conducted, it is concluded that the vaccine formulation did not produce any adverse effects at dose level of 0.5 mL. Immunogenicity studies are also conducted with the vaccine in Rats and Rabbits. Based on the immunogenicity studies, the vaccine showed IgG response to individual serotypes PnCPS in the vaccine formulation.

6. Pharmaceutical Particulars

The vaccine contains Streptococcus pneumoniae serotypes 1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F and 33F.

6.1. List of Excipients
- Aluminium Phosphate as Al+++
- 2 Phenoxyethanol (as preservative in multi dose presentation)

Other Ingredients:
- Polysorbate 20
- Succinic Acid

6.2. Incompatibilities

The product should not be mixed with any other medicinal products or active immunizing agents.

6.3. Shelf Life

24 months from the date of manufacturing. The manufacturing date and expiry date of the vaccine is indicated on the label and carton of the product.

6.4. Special precautions for Storage
Store at +2°C to +8°C. DO NOT FREEZE. Discard if found frozen. Shake vigorously before use. Keep out of reach of children.

Handling of multidose vial once opened:
Once opened, multi-dose vials should be kept between +2°C and +8°C. Multi-dose vials of Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (14-valent) from which one or more doses of vaccine have been removed during an immunization session may be used in subsequent immunization sessions for up to a maximum of 28 days, provided that all of the following conditions are met:

- The vaccine is approved for use for up to 28 days after opening the vial
- The expiry date has not passed
- The vaccine vial has been, and will continue to be, stored at manufacturer recommended temperatures; furthermore, the vaccine vial monitor if one is attached, is visible on the vaccine label and is not past its discard point, and the vaccine has not been damaged by freezing.

6.5. Nature and contents of container
BE-PCV14 is filled in USP type I glass vials and closed using bromobutyl rubber stoppers and sealed with aluminium flip-off seals.
The vaccine is filled in to single dose and five dose presentations and is offered in the following presentations:

- Single dose Vial of 0.5 mL
- Multi dose Vial of 2.5 mL

The above presentations are offered in different packaging configuration as per the requirement. Not all pack sizes may be marketed.

6.6. Special precautions for disposal
Any unused product or waste material should be disposed of in accordance with local requirements

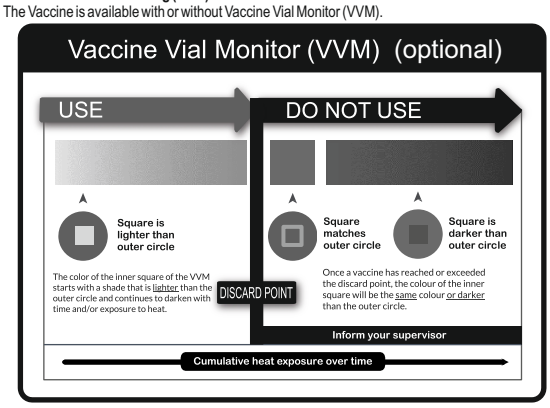
6.7. Patient Counselling Information
BE-PCV14 is a conjugate vaccine containing polysaccharides from serotypes 1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F, and 33F conjugated to non-toxic diphtheria toxin cross-reacting material (CRM_{197}) The body is expected to develop an immune response against the injected 197 serotypes which would help in prevention of disease caused by Streptococcus pneumoniae. Most common adverse events that have been reported with the BE-PCV14 are injection site pain or tenderness. Other common systemic adverse events reported are fever and injection site redness. There is a remote chance that BE-PCV14 could cause a severe allergic reaction. A severe allergic reaction may very rarely occur after getting a dose of BE-PCV14. For this reason, your vaccination provider will ask you to stay for 30 minutes after each dose of vaccination at the place where you received your vaccine for monitoring after vaccination.
Signs of a severe allergic reaction can include:

- Difficulty in breathing
- Swelling of your face and throat
- A fast heart beat
- Rash all over your body
- Dizziness and weakness

If the vaccinee experiences any of the above side effect(s), please contact or visit your health care provider / vaccinator / officer supervising your vaccination or immediately go to the nearest hospital.

7. Instructions for use, handling and disposal
Each vaccine dose of 0.5 mL is withdrawn into a syringe for injection to be administered intramuscularly. Use a separate sterile needle and syringe for each individual.

7.1. Vaccine Vial Monitoring (VVM)
The Vaccine is available with or without Vaccine Vial Monitor (VVM).



VVM is a label containing a heat- sensitive material which is placed on a vaccine vial to register cumulative heat exposure over time. The colour dot appears on the VVM label in square element is a time - temperature sensitive dot that provides an indication of the cumulative heat to which the vial has been exposed. It warns the end user when exposure to heat is likely to have degraded the vaccine beyond an acceptable level.
The interpretation of the VVM is simple. Focus on the central square. Its colour will change progressively. As long as the colour of this square is lighter than the colour of the ring, then the vaccine can be used. As soon as the colour of the central square is the same colour as the ring or of a darker colour than the ring, then the vial should be discarded.

8. Details of manufacturer

Biological E. Limited

Registered office:
18/1 & 3, Azamabad, Hyderabad, Telangana - 500 020, INDIA.

Manufacturing Site Address:
SEZ Unit, Sy.No. 549, 550, 552 to 556, Kolthur Village, Shameerpet,
Medchal-Malkajgiri district, Telangana, India - 500 078.
Web site: www.biologicale.com
® - Registered Trade Mark

9. Details of permission or licence number with date
Permission No: MF/BI0/22/000112
Date of issue: 10-Dec-2022

10. Date of revision
Oct 2025

You can help by reporting any side effects that you may get after vaccination to Biological E. Limited (BE), who is the manufacturer of **PNEUBEVAX 14®** on:
E-mail at pharmacovigilance@biologicale.com
For adverse event reporting online: https://www.biologicale.com
For more information, read this Package Insert carefully.

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Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (14 Valent)

PNEUBEVAX 14®

1. Name of the Medicinal Product
Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (14-valent)

2. Composition
Single Dose (0.5 mL) Presentation:
Each dose of 0.5 mL contains:
Single Dose (0.5 mL) Presentation:
Each dose of 0.5 mL contains:

Pneumococcal polysaccharide serotype 1	3.0 µg
Pneumococcal polysaccharide serotypes 3, 4, 5, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F and 33F (each)	2.2 µg
Pneumococcal polysaccharide serotype 6B	4.4 µg
Adsorbed onto Aluminium Phosphate, as Al^{+++}	≤ 0.75 mg
Polysaccharides conjugated to 20-50 µg of CRM_{197}	

Multi Dose (2.5 mL) Presentation:
Each dose of 0.5 mL contains:

Pneumococcal polysaccharide serotype 1	3.0 µg
Pneumococcal polysaccharide serotypes 3, 4, 5, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F and 33F (each)	2.2 µg
Pneumococcal polysaccharide serotype 6B	4.4 µg
Adsorbed onto Aluminium Phosphate, as Al^{+++}	≤ 0.75 mg
2- Phenoxyethanol	4 mg
Polysaccharides conjugated to 20-50 µg of CRM_{197}	

3. Pharmaceutical Form
BE-PCV14 is a whitish suspension in which the mineral carriers tend to settle down slowly. The vaccine contains *Streptococcus pneumoniae* serotypes 1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F and 33F. These polysaccharides are conjugated using CRM_{197}. The antigens are adsorbed onto Aluminium Phosphate as an adjuvant. 2-Phenoxyethanol is used as preservative only in multi-dose presentation.

4. Clinical Particulars
4.1. Therapeutic Indications
BE-PCV14 is indicated for active immunization against invasive diseases, pneumonia and otitis media caused by *Streptococcus pneumoniae* serotypes 1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F, 33F and cross reactive 6A, in children from 6 weeks of age.

4.2. Posology and Method of Administration
BE-PCV14 is to be administered as a three dose primary series in infants at 6-10-14 weeks or a two dose primary series at 6 weeks-14 weeks with a booster at 9 months.
The vaccine should be administered intramuscularly. The preferred site is anterolateral aspect of the upper thigh. The vaccine should not be injected in the gluteal area. Use a separate sterile needle and syringe for each individual. The vaccine should not be injected intradermally, subcutaneously or intravenously, since the safety and immunogenicity of these routes have not been evaluated.

Vaccination schedule for infants				
Dosage schedule	6 weeks	10 weeks	14 weeks	9 months*
3p+0	Dose 1	Dose 2	Dose 3	–
2p+1	Dose 1	–	Dose 2	Dose 3
Dose 1 can be given as early as 6 weeks of age The recommended dosing interval for primary series is 4 to 8 weeks *Booster dose is recommended at 9 months of age p:primary dose				

For children who are beyond the age of routine infant schedule, the National Recommendation should be followed.
The vaccine vial should be shaken vigorously to obtain a uniform suspension before use. Prior to administration, the vaccine vial should be visually checked for complete suspension and/or presence of any particulate matter. In the event of either being observed, discard the vaccine. Sterile needle and syringe should be used for withdrawal of the vaccine.

4.3. Contraindications
Hypersensitivity to any constituents of the vaccine listed in section 6.1

4.4. Special Warnings and Precautions for Use

- Do not administer intravenously, intradermally, or subcutaneously.
- Like all other vaccines, supervision and appropriate medical treatment should always be available to treat any anaphylactic reactions following immunization
- **The vaccinee should remain under medical supervision for at least 30 minutes after vaccination**
- **Concurrent illness**: As with other vaccines, administration of BE-PCV14 should be postponed in individuals suffering from an acute severe febrile illness.
- Adrenaline Injection (1:1000) should be available in case of acute Anaphylactic reaction following vaccination.
- **Thrombocytopenia and coagulation disorders**: As with any other intramuscular injection, BE-PCV14 should be given with caution in individuals with thrombocytopenia and coagulation disorders or to individuals on treatment with anticoagulation therapy, because of risk of bleeding or bruising following an intramuscular injection in these individuals.
- **Immunocompromised individuals**: it is not known if individuals with impaired immune responsiveness, including individuals receiving immunosuppressant therapy, will elicit the same response as immunocompetent individuals to BE-PCV14. These individuals may have a weaker immune response to the vaccine.

SPECIAL POPULATIONS:
Currently, safety and immunogenicity data for the BE's 14-valent Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) are not available for children belonging to specific high-risk groups for invasive pneumococcal disease—such as those with congenital or acquired splenic dysfunction, HIV infection, malignancies, or nephrotic syndrome. These children may exhibit a diminished antibody response to active immunization due to compromised immune function. Although limited, existing data on other pneumococcal conjugate vaccines suggest that they can elicit an immune response in children with HIV, sickle cell disease, and in premature infants, with safety profiles comparable to those seen in children not considered high risk. Use of the BE's 14-valent Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) in high-risk pediatric groups should be evaluated on a case-by-case basis, taking individual clinical circumstances into account.
Premature Infants: Experience with other pneumococcal conjugate vaccines suggests a potential risk of apnoea following vaccination in very premature infants (born at ≤28 weeks gestation), particularly in those with a history of respiratory immaturity. Therefore, consideration should be given to monitoring respiratory function for 48 to 72 hours after administration of the primary immunization series in this population. BE-PCV14 has not been studied in premature infants in the clinical trials. As the benefit of vaccination is high in this group of infants, vaccination with Pneumococcal Polysaccharide conjugate vaccine (Adsorbed) (14-valent) should not be withheld or delayed.

4.5. Drugs interactions
BE-PCV14 can be given with either monovalent or combination vaccines containing diphtheria, tetanus, whole-cell pertussis, hepatitis B, *Haemophilus influenzae* type b, inactivated or oral poliomyelitis and Rotavirus vaccine. Clinical studies demonstrated that the safety and immunogenicity profiles of the administered vaccines were unaffected. For concomitant administration, use different injection sites and separate syringes.

4.6. Use in special populations (such as pregnant women, lactating women)
Safety and effectiveness have not been established in pregnant women, nursing mothers. It is not known whether the vaccine is excreted in human milk.

4.7. Effect on ability to drive and use machines

No studies on the effect of BE-PCV14 on the ability to drive and use machines have been performed.

4.8. Undesirable effects

Clinical Trial Experience: The safety of BE's Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) I.P. (14 Valent) [BE-PCV14] was established in 6-8-week-old infants in 6-10-14 weeks primary schedule, 6 weeks-14 weeks and 9 months schedule,12-23 months old toddlers and 18-45-year-old adult individuals. Within each system organ class (SOC) the adverse reactions were ranked under headings using the following convention:

Expected frequency of adverse events in vaccinees

Very common	≥ 10%
Common	≥ 1% and < 10%
Uncommon	≥ 0.1% and < 1%
Rare	≥ 0.01% and < 0.1%
Very rare	≤ 0.01%

Systemic:

Common (≥ 1% and < 10%)
- Fever/Pyrexia
- Irritability Postvaccinal
- Diarrhoea

Uncommon (≥ 0.1% and < 1%)
- Chills
- Crying
- Decreased appetite
- Somnolence
- Vomiting

Local:

Very common (≥ 10%)
- Injection site pain (tenderness)

Common (≥ 1% and < 10%)
- Injection site erythema
- Injection site induration/swelling

Summary of safety profile:

In the Phase I study (BECT043), conducted in 24 healthy adult subjects aged 18 to 45 years, the most commonly reported local adverse events were injection site pain, erythema, and tenderness. All local reactions were assessed as related to the study vaccine. The most frequently reported systemic adverse events included chills, headache, fever (pyrexia), and rash. According to the principal investigator, all systemic adverse events were considered vaccine-related.

In the Phase II study (BECT044), 120 healthy, pneumococcal vaccine-naïve Indian toddlers aged 12 to 23 months were enrolled and randomized in a 1:1 ratio to receive either BE-PCV14 or a licensed 13-valent pneumococcal conjugate vaccine as a comparator. In the BE-PCV14 group, the most frequently reported treatment-emergent adverse events (by preferred term) included injection site pain, pyrexia, injection site swelling, erythema/redness at the injection site, crying, and decreased appetite.

In the controlled Phase-III (BECT051) study conducted in 1290 infants of 6-8 weeks old in 6-10-14 weeks dosing schedule, randomized in 1:1 ratio between BE-PCV14 or 13 valent licensed comparator, the safety profile of BE-PCV14 was comparable to the licensed PCV in terms of overall AE rates, related AE rates and medically attended AEs. The total number of subjects with at least one adverse event reported in BE-PCV14 group were 175/645 (27.1%) as against 178/645 (27.6%) in the licensed comparator group. The number of subjects reporting at least one adverse event were similar in BE-PCV14 and licensed comparator groups. Out of total 1290 enrolled subjects, 175/645 (27.1%) subjects reported 355 events and 178/645 (27.6%) subjects reported 353 events in BE-PCV14 and licensed comparator groups respectively. The most frequently reported adverse events in BE-PCV14 group were Injection site pain [133 AEs in 93 (14.4%) subjects], Pyrexia [53 AEs in 42 (6.5%) subjects], Injection site swelling [51 AEs in 44 (6.8%) subjects], Injection site erythema [38 AEs in 33 (5.1%) subjects], Irritability postvaccinal [41 AEs in 25 (3.9%) subjects], Injection site induration [13 AEs in 9 (1.4%) subjects], Decreased appetite [9 AEs in 8 (1.2%) subjects], Diarrhoea [8 AEs in 6 (0.9%) subjects], Vomiting [3 AEs in 3 (0.5%) subjects] and Somnolence [4 AEs in 2 (0.3%) subjects]. The most frequently reported adverse events in licensed comparator group were Injection site pain [131 AEs in 98 (15.2%) subjects], Pyrexia [51 AEs in 40 (6.2%) subjects], Injection site swelling [58 AEs in 48 (7.4%) subjects], Injection site erythema [44 AEs in 36 (5.6%) subjects], Irritability postvaccinal [31 AEs in 21 (3.3%) subjects], Injection site induration [18 AEs in 13 (2.0%) subjects], Decreased appetite [10 AEs in 6 (0.9%) subjects], Vomiting [5 AEs in 4 (0.6%) subjects], Diarrhoea [3 AEs in 2 (0.3%) subjects] and Somnolence [2 AEs in 1 (0.2%) subjects].

In another controlled Phase-III (BECT061) study conducted in 300 infants of 6-8 weeks old in 6-10-14 weeks dosing schedule, randomized in 1:1 ratio between BE-PCV14 or 13-valent licensed comparator, the safety profile of BE-PCV14 was comparable to the control vaccine licensed comparator in terms of overall AE rates, related AE rates and medically attended AEs. The most frequently reported adverse events in BE-PCV14 group were Injection site pain [24 AEs in 17 (11.3%) subjects], Injection site swelling [14 AEs in 10 (6.7%) subjects], Injection site erythema [10 AEs in 10 (6.7%) subjects], Irritability postvaccinal [12 AEs in 5 (3.3%) subjects], Pyrexia [5 AEs in 5 (3.3%) subjects] and Injection site induration [1 AE in 1 (0.7%) subject]. The most frequently reported adverse events in licensed comparator group were Injection site pain [25 AEs in 19 (12.7%) subjects], Injection site swelling [16 AEs in 13 (8.7%) subjects], Pyrexia [13 AEs in 12 (8.0%) subjects], Irritability postvaccinal [9 AEs in 6 (4.0%) subjects], Injection site erythema [7 AEs in 7 (4.7%) subjects] and Vomiting [1 AE in 1 (0.7%) subject].

Across both Phase III studies, all reported adverse events were of mild to moderate intensity. The majority of AEs were assessed by investigators as related to the study vaccine and were solicited in nature. No severe adverse events, serious adverse events (SAEs), or deaths were reported in either treatment group. There were no clinically meaningful changes observed in vital signs or physical examination findings over time, and no safety concerns were identified based on AE profiles.

In a Phase-III (BECT056) study conducted in 400 infants of 6-8 weeks old in 6weeks, 14 weeks and 9 months (2p+1) dosing schedule, randomized in 1:1 ratio between BE-PCV14 or 13-valent licensed comparator, the safety profile of BE-PCV14 was comparable to the control vaccine licensed comparator in terms of overall AE rates, related AE rates and medically attended AEs. The most frequently reported adverse events in Biological E's 14-valent pneumococcal polysaccharide conjugate vaccine group were Injection site pain [34 (17.50%) subjects with 38 events], Pyrexia [28 (14.00%) subjects with 31 events], Injection site swelling [12 (6.00%) subjects with 12 events] and Injection site erythema [11 (5.50%) subjects with 12 events], Injection site induration [7 (3.50%) subjects with 7 events], Irritability postvaccinal [4 (2.50%) subjects with 4 events], Vomiting [2 (1.00%) subjects with 2 events], Diarrhoea [1 (0.50%) subject with 1 event] and Somnolence [1 (0.50%) subject with 1 event]. The reported AEs were predominantly mild to moderate in severity, and no safety concerns were identified. The results further support the favourable safety profile of BE-PCV14 when administered in a 2p+1 dosing schedule.

In a post marketing, Phase IV study (BECT081) conducted to evaluate the safety of BE- PCV14 administered in a 6-10-14-week dosing schedule to healthy Indian infants aged 6–8 weeks, 26.30% of the 2300 infants who received BE-PCV14 reported adverse events compared to 24.67% of the 300 infants who received licensed comparator vaccine during study period dose 1 to one month after dose 3 (i.e day 84).

The most commonly reported adverse events in BE-PCV14 arm were Pyrexia (14.04% recipients), Injection site pai (10.96% recipients), Injection site swelling (6.35% recipients), Injection site erythema (4.52% recipients), Irritability postvaccinal (2.96% recipients), Injection site Induration (1.78% recipients), Decreased appetite (0.96% recipients) and Diarrhoea (0.96% recipients). In licensed comparator arm, the most commonly reported adverse events were Pyrexia (10.33% recipients), Injection site pain (8.67% recipients), Injection site erythema (5.00% recipients) and Injection site swelling (4.00% recipients).

Adverse Events Reported from day 84 to 6-Month Follow-up Visit:

During the 6-month follow-up period, 1.78% of the participants in the BE-PCV14 arm and 1.00% in the licensed comparator arm reported adverse events. The most commonly reported adverse events in the BE's PCV14 arm were pyrexia (0.78% recipients), vomiting (0.35% recipients), nasopharyngitis (0.26% recipients), and diarrhoea 0.13% (recipients). In the licensed comparator arm, the most commonly reported adverse events were pyrexia (0.67% recipients) and cough (0.33% recipients)

Majority of the reported adverse events were mild in intensity and considered related to the study vaccine. The nature and pattern of adverse events observed were consistent with the known safety profile of other licensed pneumococcal conjugate vaccines.

4.9. Overdose

No case of overdose has been reported. There is no specific treatment for an overdose with BE-PCV14. In the event of an overdose, the individual should be monitored and provided with symptomatic treatment as appropriate.

5. Pharmacological Properties

5.1. Pharmacodynamic Properties

Mechanism of Action

Streptococcus pneumoniae causes paediatric invasive bacterial disease (including bacteraemia, bacterial pneumonia and meningitis), and non-invasive disease (pneumonia and acute otitis media) and is estimated to account for approximately 1 million deaths per year worldwide among children younger than 5 years of age.

Unconjugated bacterial polysaccharides stimulate B cells through a T cell-independent mechanism, resulting primarily in the production of IgM antibodies, which are short-lived. Generally, there is no affinity maturation of the antibodies, and no memory cells are produced, leading to the absence of a booster response to subsequent doses of the same antigen. Conjugation of bacterial polysaccharides to a protein (such as CRM_{197}) results in a T cell-dependent immune response, in which CD4+ T-helper cells activate B cells to proliferate and differentiate into plasma cells. These plasma cells produce IgG antibodies and memory B cells. Affinity maturation leads to the production of high-affinity IgG antibodies, while the presence of memory B cells enables rapid mobilization and antibody secretion upon re-exposure to the same antigen (booster response). Unlike polysaccharide vaccines, which have poor or no immunogenicity in infants and toddlers under 2 years of age, conjugate vaccines are immunogenic across all age groups, including infants and toddlers younger than 24 months. Conjugating *Streptococcus pneumoniae* polysaccharides to the CRM_{197} protein enhances the antibody response, induces long-lasting immune memory, and elicits a booster response upon re-exposure to the same polysaccharide antigen in infants and young children.

BE-PCV14 contains polysaccharides from serotypes 1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F and 33F conjugated to non-toxic diphtheria toxin cross-reacting material (CRM_{197}) providing broader coverage. Serotypes 22F and 33F are added in the BE-PCV14 since these serotypes have emerged as important causes of invasive pneumococcal disease (IPD), particularly in the post-PCV13 era, due to serotype replacement. These serotypes are now among the leading causes of IPD in several regions, especially in infants, older adults, and immunocompromised individuals. Including 22F and 33F in pneumococcal conjugate vaccines broadens protection against strains not covered by earlier-generation vaccines, helping to address the evolving epidemiology of pneumococcal disease and reduce residual disease burden. Their inclusion is supported by surveillance data and aligns with public health goals to enhance effectiveness of pneumococcal conjugate vaccines.

The body develops an immune response against the injected serotypes which would help in prevention of disease caused by *Streptococcus pneumoniae*.

In the clinical trials conducted in healthy infants and toddlers, the vaccine was found to be safe and immunogenic.

Efficacy and Immunogenicity data

In the Phase-II (BECT044) comparative study conducted in 120 subjects aged 12-23 months, randomized in 1:1 ratio between BE-PCV14 or 13 valent licensed comparator given as 2 doses with 2 months apart, the proportion of subjects seroconverted one month after two doses were 96.55% (56), 98.28% (57), 100% (58), 100% (58), 93.10% (54), 100% (58), 100% (58), 100% (58), 100% (58), 98.28% (57), 100% (58), 98.28% (57), 100% (58) and 91.38% (53) against serotypes 1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F and 33F respectively. The immunogenicity of BE-PCV14 was found to be comparable to that of the licensed 13-valent comparator across all shared serotypes and demonstrated robust responses to the additional serotypes 22F and 33F.

In the Phase-III (BECT051) study conducted in 1290 infants of 6-8 weeks old in 6-10-14 weeks dosing schedule, randomized in 1:1 ratio between BE-PCV14 or 13-valent licensed comparator, the proportion of subjects seroconverted at visit 3 (Day 86) were 90.6% (581), 83.5% (535), 93.1% (597), 90.6% (581), 76.3% (489), 95.8% (614), 95.2% (610), 99.7% (639), 90.5% (580), 99.4% (637), 97.2% (623), 94.1% (603), 82.4% (528) and 73.2% (469) against serotypes 1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F & 33F respectively. BE-PCV14 demonstrated immunogenic non-inferiority to licensed 13 valent PCV w.r.t seroconversion rate and Geometric mean concentration ratio for all shared serotypes. The vaccine also induced robust OPA antibodies which were comparable to licensed comparator vaccine.

In another Phase-III (BECT061) study conducted in 300 infants of 6-8 weeks old in 6-10-14 weeks dosing schedule, randomized in 1:1 ratio between BE-PCV14 or 13-valent licensed comparator, the proportion of subjects seroconverted at visit 3 (Day 86) were 93.3% (139), 76.5% (114), 91.3% (136), 88.6% (132), 81.2% (121), 96.6% (144), 94.6% (141), 100.0% (149), 91.3% (136), 100.0% (149), 97.3% (145), 88.6% (132), 86.6% (129) and 67.1% (100) against serotypes 1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F & 33F respectively.

The immune response to serotype 6A was achieved through cross protection from serotype 6B with BE-PCV14, which is evident from two phase III clinical studies.

In Phase III (BECT056) study conducted in 400 infants of 6-8 weeks old in 6weeks, 14weeks and 9 months (2p+1) dosing schedule, randomized in 1:1 ratio between BE-PCV14 or 13-valent licensed comparator, the proportion of subjects seroconverted at Day 84 were Serotype 1 (98.4 %), Serotype 3 (72.6%), Serotype 4 (94.6%), Serotype 5 (94.6%), Serotype 6A (70.4%), Serotype 6B (85.5%), Serotype 7F (97.8%), Serotype 9V (96.8%), Serotype 14 (100%), Serotype 18C (88.7%), Serotype 19A (99.5%), Serotype 19F (100%), Serotype 23F (89.2%), Serotype 22F (95.2%), Serotype 33F (81.2%%).

Day 270 (pre-booster) Serotype 1 (84.9%), Serotype 3 (57%), Serotype 4 (67.7%), Serotype 5 (66.1%), Serotype 6A (69.3%), Serotype 6B (90.9%), Serotype 7F (79.6%), Serotype 9V (69.9%), Serotype 14 (100%), Serotype 18C (55.9%), Serotype 19A (96.2%), Serotype 19F (99.5%), Serotype 23F (70.4%), Serotype 22F (98.9%), Serotype 33F (85.5%).

Day 300 (post-booster) Serotype 1 (97.8%), Serotype 3 (87.6%), Serotype 4 (92.5%), Serotype 5 (91.9%), Serotype 6A (93.0%), Serotype 6B (97.3%), Serotype 7F (95.7%), Serotype 9V (94.6%), Serotype 14 (100%), Serotype 18C (89.2%), Serotype 19A (98.9%), Serotype 19F (99.5%), Serotype 23F (93.5%), Serotype 22F (96.8%), Serotype 33F (92.5%).

BE-PCV14 demonstrated comparable immune response to licensed 13 valent comparator vaccine in 2p+1 schedule for all shared serotypes. Immune response to serotypes 22F, 33F and 6A was also demonstrated. Both vaccines demonstrated good persistence of antibody responses at day 270 (pre-booster) and robust booster responses at day 300 (30 days post booster), indicating successful priming and development of immunological memory.

BE-PCV14 has shown comparable seroconversion rates and serotype specific anti-PnCPS IgG antibody concentrations for the common serotypes of the 13 valent licensed comparator in all the studies conducted so far.

5.2. Pharmacokinetic Properties

Evaluation of pharmacokinetic properties is not required for vaccines.

5.3. Preclinical safety data

Animal Toxicology or Pharmacology:

Single dose toxicity studies in Rats and repeat dose toxicity studies in Rats and Rabbits were conducted. Based on the toxicity studies conducted, it is concluded that the vaccine formulation did not produce any adverse effects at dose level of 0.5 mL. Immunogenicity studies are also conducted with the vaccine in Rats and Rabbits. Based on the immunogenicity studies, the vaccine showed IgG response to individual serotypes PnCPS in the vaccine formulation.

6. Pharmaceutical Particulars

The vaccine contains Streptococcus pneumoniae serotypes 1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F and 33F.

6.1. List of Excipients
- Aluminium Phosphate as Al+++
- 2 Phenoxyethanol (as preservative in multi dose presentation)

Other Ingredients:
- Polysorbate 20
- Succinic Acid

6.2. Incompatibilities

The product should not be mixed with any other medicinal products or active immunizing agents.

6.3. Shelf Life

24 months from the date of manufacturing. The manufacturing date and expiry date of the vaccine is indicated on the label and carton of the product.