PRESCRIBING INFORMATION FOR PNEUMOCOCCAL POLYSACCHARIDE VACCINE I.P. (23 VALENT)

FOR THE USE OF A REGISTERED MEDICAL PRACTITIONER OR A HOSPITAL OR A LABORATORY ONLY

1. GENERIC NAME OF THE VACCINE:

Generic name : Pneumococcal Polysaccharide Vaccine I.P. (23 valent)

Pharmaceutical Form : Injection

This vaccine is a clear, colourless solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Each dose of 0.5 mL contains

Raw Material	Quantity	Function
Active Ingredient		
Type 1 Pneumococcal Polysaccharide	25 μg	Antigen
Type 2 Pneumococcal Polysaccharide	25 μg	Antigen
Type 3 Pneumococcal Polysaccharide	25 μg	Antigen
Type 4 Pneumococcal Polysaccharide	25 μg	Antigen
Type 5 Pneumococcal Polysaccharide	25 μg	Antigen
Type 6B Pneumococcal Polysaccharide	25 μg	Antigen
Type 7F Pneumococcal Polysaccharide	25 μg	Antigen
Type 8 Pneumococcal Polysaccharide	25 μg	Antigen
Type 9N Pneumococcal Polysaccharide	25 μg	Antigen
Type 9V Pneumococcal Polysaccharide	25 μg	Antigen
Type 10A Pneumococcal Polysaccharide	25 μg	Antigen
Type 11A Pneumococcal Polysaccharide	25 μg	Antigen
Type 12F Pneumococcal Polysaccharide	25 μg	Antigen
Type 14 Pneumococcal Polysaccharide	25 μg	Antigen
Type 15B Pneumococcal Polysaccharide	25 μg	Antigen
Type 17F Pneumococcal Polysaccharide	25 μg	Antigen
Type 18C Pneumococcal Polysaccharide	25 μg	Antigen
Type 19A Pneumococcal Polysaccharide	25 μg	Antigen
Type 19F Pneumococcal Polysaccharide	25 μg	Antigen
Type 20 Pneumococcal Polysaccharide	25 μg	Antigen
Type 22F Pneumococcal Polysaccharide	25 μg	Antigen
Type 23F Pneumococcal Polysaccharide	25 μg	Antigen
Type 33F Pneumococcal Polysaccharide	25 μg	Antigen
Inactive ingredients		
Sodium Dihydrogen Phosphate	30 μg	Maintenance osmotic pressure
Disodium Hydrogen Phosphate	35.5 μg	Maintenance osmotic pressure
Sodium Chloride	4.25 mg	Maintenance osmotic pressure
Water for injection	To 0.5 mL	Diluent

Total amount of polysaccharide per PFS = 632.5 μg/0.55 mL

3. DOSAGE FORM:

Solution for intramuscular route of administration

4. CLINICAL PARTICULARS

4.1. THERAPEUTIC INDICATION:

It is a vaccine indicated for active immunization for the prevention of pneumococcal disease caused by the 23 serotypes contained in the vaccine (1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20, 22F, 23F and 33F).

This vaccine is proposed for use in adults aged 18 to 65 years when administered in single dose of 0.5 mL.

4.2. POSOLOGY AND METHOD OF ADMINISTRATION:

- Injection site and route: Administer intramuscularly into the deltoid muscle of the lateral upper arm.
- Dosage: Single dose (0.5 mL) Pre-filled Syringe.

4.3. CONTRAINDICATIONS:

PPSV 23 should not be administered to:

- Individuals with allergic reactions to any component of the vaccine.
- Subjects with encephalopathy, uncontrolled epilepsy, or other progressive disease of nervous system.
- Subjects with fever, acute infection, chronic disease at stage of acute attack.

4.4. SPECIAL WARNINGS & PRECAUTIONS FOR USE:

- Do not administer subcutaneously or intradermal or intravenously routes, and ensure the needle not penetrated in the blood vessel.
- The vaccine shall be administered with caution to the subjects with family or individual history of convulsion, history of epilepsy, allergic diathesis, and nursing women.
- Check the container for package, label, validity period meeting the requirements. Do not use the vaccine if the container shows abnormalities, such as crack, label missing, foreign matters, vaccine turbid or change color, and exceed validity period.
- The vaccine with the entire contents shall be administered immediately after the container is opened.
- Adrenaline should be available for first aid in case of severe anaphylactic reactions. The recipient shall be observed for at least 30 minutes on site following injection.
- Freezing is strictly forbidden.

4.5. DRUG INTERACTIONS:

PPSV 23 is not recommended to be given concurrently with other vaccine.

4.6 PREGNANCY AND LACTATION:

It is not known whether PPSV 23 can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. PPSV 23 should be given to pregnant women only if clearly needed. It is not known whether this vaccine is excreted in human milk. Caution should be exercised when administered to a nursing mother.

4.7. EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

No studies on the effects on the ability to drive and use machines have been performed with PPSV 23.

4.8. UNDESIRABLE EFFECTS:

According to the adverse reactions reported in domestic clinical trials, the rates of adverse reactions, as Council for International Organizations of Medical Sciences (CIOMS) recommends, are extremely common (≥10%), common (1% ~10%, including 1%), uncommon (0.1% ~ 1%, including 0.1%), rare (0.01% ~ 0.1%, including 0.01%), extremely rare (< 0.01%) which are described as follows:

Extremely common:

Injection-site pain (mild and transient).

Common:

- Injection-site reactions: erythema, swelling, pruritus.
- Systemic reactions: Fever, fatigue, headache, diarrhea.

Uncommon:

- Injection-site reactions: induration
- Systemic reactions: vomiting, skin rash, allergy.

The following adverse reactions are observed in the use of the same category of vaccine:

- Cellulitis, the reported reaction usually occurs quickly following vaccination in post marketing use.
- Hypersensitivity reactions: including anaphylactoid reactions, serum sickness, angioneurotic edema.
- Nervous system: radiculoneuritis, Guillain-Barre syndrome, febrile convulsion.
- Hematologic/ lymphatic system: lymphadenitis, lymphadenopathy, thrombocytopenia in patients with stabilized idiopathic thrombocytopenic purpura, thrombocytopenia, hemolytic anemia in patients who have had other hematologic disease, leukocytosis.
- Rare Arthus phenomenon, also reported, can completely resolve, leaving no sequela, usually seen in patients with high levels of pneumococcal antibodies.
- Wide spreaded skin rash and ulticaria
- Myalgia, arthralgia

If any adverse reactions not included above occur after administering this vaccine, please contact and report to your physician.

4.9. OVERDOSE:

Not applicable

5. PHARMACOLOGICAL PROPERTIES

5.1. PHARMACODYNAMIC PROPERTIES

A total of 1660 subjects were enrolled in the pivotal clinical trial which consists of two stages. The design of this two-stage pivotal clinical trial regarded the first stage as phase I and the second stage as phase III in the study protocol whereas the results were concluded together in clinical study report of the pivotal study report.

A total of 60 subjects were enrolled in the first stage (Phase I) clinical trial which was aimed for preliminarily stepwise safety observation from adults ≥18 years to children aged 2-17 years. 30 adults aged ≥18 were enrolled firstly and administrated with 1 dose of PPSV23 vaccine. On the premise that there was no serious adverse event related to vaccination within 30-minute and 0-7- day post-immunization in adult subjects, 30 children aged 2-17 were then enrolled, and safety within 30-minute and 0-7-day after 1 does of immunization were observed as well. As a summary for the phase I study, in both subjects ≥ 18 years and 2-7 years, no serious adverse event related to the study vaccine was observed.

The endpoint of phase I clinical trials was reached, which facilitated the second stage (phase III) clinical trial in the expanded population according to the protocol.

The remaining 1600 subjects were enrolled in the second stage of the pivotal clinical trial and equally divided into the study group and control group and randomized to four age groups, including 250 subjects of 2~6 old of age, 250 subjects of 7~17 old of age, 600 subjects of 18~59 old of age and 500 subjects aged 60 or above.

The antibody geometric mean concentrations (GMCs) of 23 serotypes in the test group ranged from 3.55 to 36.96, there was no significant difference between the test group and control group, nor was there any significant difference in each serotype GMC before vaccination.

The double increase rates of antibody concentration for all serotypes reached non-inferiority for the test group compared to the control group. The antibody GMCs and rates for antibody fold increase for 22 serotypes except 6B in the test group were significantly higher or not lower than those in the control group. For 6B, the antibody GMC and rate for antibody fold increase in the test group were a little bit lower than the control group, but still kept at a normal level.

5.2.PHARMACOKINETIC PROPERTIES

Not applicable

6. NONCLINICAL PROPERTIES

6.1. ANIMAL TOXICOLOGY AND PHARMACOLOGY: TOXICOLOGY:

In the allergen test in guinea pigs, we used 30 healthy guinea pigs weigh 250g-350g as subjects, and set up test group, positive control group and negative control group respectively. For test group, 6 guinea pigs were injected with this vaccine for 3 times respectively on the day 0, 2 and 4, each guinea pig was intraperitoneal injected with 0.5 mL of the finished product for sensitization test each time; 14 days after the first injection, the guinea pigs were intravenous injected with 1.0 mL of the same batch of the finished product for provocation. For positive control group, the guinea pigs were injected in the same way with the calf serum. For negative control group, the guinea pigs were injected in the same way with normal saline. The guinea pigs were observed for 30 minutes for abnormal reactions and the healthy status of the guinea pigs were observed for 7 days continuously. The test results showed that this vaccine did not contain any allergens, and the guinea pigs in the test group gained weight and didn't have any abnormal reaction. The data indicates that the product is safe and effective.

In acute toxicity in mice, we used health mice weigh 17-22g and random grouped them into 2 groups during test-- 10 mice in each group. According to the clinical concentration, the maximum intramuscular injection dose volume for mouse muscle is 10 mL/kg. We intramuscular injected the mice in the test group with this vaccine and the mice in the control group with normal saline. The results showed that the appearances, physical signs, mental and movement status of all the mice were normal. All natural holes were clean, and there was no obvious abnormal reaction observed. Compared with the control group, there was no abnormal weight change in the test group at each time point. The results showed that after intramuscularly injecting with 10 mL/kg of this vaccine, the Kunming mice were in good condition, without any abnormal changes in body weight or food intake; no toxic reaction occurs after administration.

In the abnormal toxicity test in guinea pigs, each guinea pig was administered at a clinical concentration of 5 mL/animal (10 times the human dose). So there were 2 guinea pigs in each group. Each guinea pig was intraperitoneal injected with 5 mL of this vaccine each time. The appearance, physical signs, general behavior, mental condition, breathing, genitals and perianal, fecal and urine, dying or dead condition, etc. were observed from the administration day, and observed continuously for 7 days. On the 7th day after administration, each guinea pig gained weight. The abnormal toxicity test of 5 mL/guinea pig (10 times the human dose) proved qualified. The test results showed that there was no toxicity introduced or added into excipients during the vaccine manufacturing process.

In conclusion, the results of toxicological tests showed that the animal safety of this vaccine produced by our company is reliable.

7. CLINICAL EVIDENCE ON INDIAN POPULATION

A randomized, double blind, parallel group, multicenter phase III clinical trial was conducted in the Indian population to demonstrate the non-inferior immunogenicity and safety of 23-valent Pneumococcal Polysaccharide Vaccine PPSV23 of G.C. Chemie Pharmie Ltd, as compared to current reference 23-valent Pneumococcal Polysaccharide vaccine in India, in 268 healthy adults aged 18 to 65 years.

Subjects were randomized to receive single dose of either a 23-valent pneumococcal polysaccharide investigational vaccine of G.C. Chemie Pharmie Ltd. or current reference 23-valent Pneumococcal Polysaccharide vaccine in India, by a single intramuscular injection (0.5 mL) in the deltoid muscle of shoulder region.

Subjects with history of pneumococcal infection, allergic reaction to vaccination, known or suspected immunodeficiency, asplenia, immunosuppressive drugs taken (like chemotherapy in last 5 years or corticosteroids in last 6 months) or blood products received in last 3 months, thrombocytopenia or bleeding disorder, asthma, diabetes mellitus, tuberculosis and anti-tuberculosis prophylaxis or ongoing therapy, malignancies, epilepsy, thyroid disorder/surgery, moderate-severe hypertension, psychosis, and pregnant and lactating women, as well as those with history of eclampsia, were excluded from the study. Subjects who have been administered any pneumococcal vaccine before, or received any live virus vaccine in 30 days preceding vaccination or subunit vaccine and inactivated vaccine in the 14 days before vaccination, and those with febrile illness (≥ 38°C) in 3 days or any acute infection/illness in last 7 days, were also excluded.

The vaccination was done on Day 0 (Visit 1). Local and systemic solicited reactions were observed immediately after vaccination (up to 30 minutes) and in 7 subsequent days (Day 0-7). Unsolicited Adverse events were also monitored for 28 days post vaccination. Blood samples were obtained from subjects at baseline/Day 0 (before first vaccination) and at the end of the study on Day 28 (follow-up visit) for immunogenicity evaluation. Immunogenicity was assessed in subjects' serum samples by analyzing anti-pneumococcal neutralizing antibodies by means of Multi-Analyte Immunodetection (MAID) assay method. The assay detected all of the 23 serotypes in the 23-valent polysaccharide vaccine (1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, and 33F). The primary endpoints for non-inferiority were antibody response at Day 28 post-vaccination:

- Percentage of subjects exhibiting a ≥ 2-fold increase in anti-pneumococcal IgG antibody level for all included 23 serotypes (1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20, 22F, 23F, and 33F) after vaccination in each group (seroconversion rate).
- Geometric mean fold increase (GMFI) and geometric mean concentration/titer (GMCs/GMTs) of IgG after vaccination in each group.

The secondary endpoints were safety endpoints:

- Incidence of systemic and local adverse reactions in healthy subjects after vaccination (up to 30 minutes) and in 7 subsequent days (Day 0-7).
- Incidence of unsolicited adverse events within 28 days after vaccination.
- Incidence of SAE during the entire study period.

Results:

In the PPSV23 group, percentage of subjects that attained ≥2-fold seroconversion rate of anti-pneumococcal antibody varied from 72.39% to 96.27% for all 23 serotypes, whereas in the reference vaccine group, the seroconversion rates varied from 70.15% to 98.51% for all 23 serotypes. Notably, the seroconversion rate for serotypes 2, 5, 7F, 8, 9N, 9V, 12F, 19F, and 23F exceeded 90% in both the vaccine groups. However, in the PPSV23 group, seroconversion rates for more serotypes, namely 22F also exceeded 90%, which was not observed for the reference vaccine group. The lower limit of 95% CI for treatment difference for all serotypes was ≥-10% (non-inferiority margin), demonstrating the investigational vaccine PPSV23 was non-inferior to the comparator reference vaccine.

For all the serotypes, post vaccination GMTs were more than pre vaccination GMTs. The Geometric mean fold increase (GMFI) in the subjects vaccinated with test vaccine were comparable with the subjects vaccinated with comparator vaccine. The Geometric Mean Ratio (GMR) obtained for PPSV23 over the reference vaccine for serotypes 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F and 33F were 0.87 or more, indicating that PPSV23 was non-inferior to the reference vaccine. The average Geometric Mean Ratio obtained for PPSV23) over the reference vaccine for all serotypes was > 1.

The total number and percentage of subjects in both groups reporting any AE (solicited or unsolicited, local or systemic) during the trial were 91 (34%). Out of this, 75 (27.9%) subjects reported solicited local AEs and 16 (5.9%) reported solicited systemic AEs. No unsolicited AEs were reported within 28 days after vaccination. No subject was withdrawn from the study due to an AE.

Local solicited AEs: Pain/Tenderness at the site of injection was reported as the most common local AE in both groups as reported by 38 (28.36%) subjects in PPSV23 group and 36 (26.87%) subjects in reference vaccine group. Redness was reported by only one subject in the reference vaccine group whereas swelling was not reported by any subject in either vaccine group.

Systemic solicited AEs: Amongst the systemic solicited AEs, fever was most commonly reported (PPSV23: 6, 4.48%; reference vaccine: 4, 2.99%), followed by body ache (PPSV23: 2, 1.49%; reference vaccine: 1, 0.75%). Fatigue/ Malaise was reported by only one subject in the reference vaccine group whereas headache was reported by only one subject in the PPSV23 group. No other systemic AEs were reported by any of the subjects in either vaccine group.

All solicited local and systemic were mild in severity except two events (pain at injections site and fever) which were reported as moderate in severity. All events were resolved. No SAE was reported/recorded during the entire study period.

The data from this immunogenicity and safety study shows that the study vaccine 23-valent Pneumococcal polysaccharide vaccine PPSV23 (G.C.Chemie Pharmie Ltd.) is immunogenic, safe and non-inferior to comparator reference vaccine after single dose in healthy Indian adults.

8. DESCRIPTION

It is a colourless and clear solution.

The antigenicity of an antigen is determined by its primary structure (molecular composition) and its advanced structure (secondary structure and higher structure), the integrity of which is seriously influenced by the solution system, including pH value, osmotic pressure, Ionic strength and etc., among them, pH is the most important factor. In order to ensure the effectiveness and safety of the product, adjust the osmotic pressure of antigen solution system to isotonic with body fluid, and adjust ionic strength within body tolerance range, buffer system is added to maintain the constant pH value of the system. Several antigens coexist in a solvent system, the antigenic solution is packed into a prefilled syringe.

9. PHARMACEUTICAL PARTICULARS

9.1 INCOMPATIBILITIES

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

9.2 SHELF-LIFE

The shelf life is 24 months when stored in Pre-filled Syringe (USP type 1 glass) at +2°C to +8°C. The expiry date of the vaccine is indicated on the label and packaging.

9.3 PACKAGING INFORMATION

Packed in prefilled syringe, 0.5 mL per syringe (borosilicate glass), sealed with a PP plunger rods with a rubber stopper. 1 syringe/box.

9.4 STORAGE & HANDLING INSTRUCTION:

Store at +2°C to +8°C, protected from light.

10. PATIENT COUNSELLING INFORMATION

- Inform the patient, parent or guardian of the benefits and risks associated with vaccination.
- Tell the patient, parent or guardian that vaccination with this vaccine may not offer 100% protection from pneumococcal infection.
- Provide the patient, parent or guardian with the vaccine information statements required with each immunization.
- Instruct the patient, parent or guardian to report any serious adverse reactions to their health care provider who in turn should report such events to the vaccine manufacturer or Importer or to CDSCO and to PvPI.

11. DETAILS OF MANUFACTURER:

M/s. Yuxi Walvax Biotechnology Co., Ltd.
Add: No. 83 South Dongfeng Road, High & New Technology Industries Development Zone, Yuxi, Yunnan, China Zip Code: 653100
Tel: +86-877-2076210, **Fax:** +86-877-2076918
Website: https://en.walvax.com

MARKETING AUTHORIZATION HOLDER OR IMPORT LICENSE HOLDER

Name: M/s. G.C. Chemie Pharmie Ltd.
Address: Bldg No. G Gala No 1 & 2 Ground Floor Global Warehousing OPP Kasturi Complex Rahnaltal Bhiwandi Thane Zone 5, Bhiwandi, Maharashtra (India) - 421302

12. DETAILS OF IMPORT LICENSE NUMBER WITH DATE

Import License number - IL/BIO-000310 - RC/BIO-000306
Dated: 01-11-2022

13. DATE OF REVISION

First version.

To report product complaint or Adverse Drug Reaction dial Toll Free no.: 18002020272 or email at adr@gccpl.com.