SINOVAC

# Poliomyelitis Vaccine (Vero Cell), Inactivated, Sabin Strains

**1.NAME OF THE MEDICAL PRODUCT**

Poliomyelitis Vaccine (Vero Cell), Inactivated, Sabin Strains

**2.QUALITATIVE AND QUANTITATIVE COMPOSITION**

**2.1 General description**

Poliomyelitis Vaccine (Vero Cell), Inactivated, Sabin Strains (sIPV) is a trivalent liquid vaccine containing a suspension of poliovirus type 1, type 2 and type 3 (Sabin strains) produced in Vero cells, concentrated, purified and inactivated, followed by the proper formulation.

The vaccine satisfies the recommendations given by the World Health Organization in *WHO TRS No. 993, Annex 3, 2015.*

**2.2 Qualitative and quantitative composition**

Suspension for injection in a glass vial. Each vial contains 2.5 mL, 5 doses per vial.

Each dose of 0.5 mL contains:

Active ingredients:

Inactivated poliovirus Type 1, Sabin* 15 DU**

Inactivated poliovirus Type 2, Sabin* 45 DU**

Inactivated poliovirus Type 3, Sabin* 45 DU**

*Produced in Vero cells

**DU: D antigen unit

For the full list of excipients, see section 6.1.

**3. PHARMACEUTICAL FORM**

Suspension for injection. The color of the vaccine varies from colorless to light yellow.

**4. CLINICAL PARTICULARS**

**4.1 Therapeutic indications**

Active immunization against poliomyelitis.

**4.2 Posology and method of administration**

Posology

Primary vaccination consists of three vaccinations, administered with a minimum interval of 4 weeks. Infants are recommended to receive the first dose at 2 months old. After completion of the primary vaccination, a booster dose is recommended to be administered at the age of 18 months. This vaccine must be used in accordance with current national recommendations and according to WHO recommendations.

Method of administration

For intramuscular injection. Recommendations about injection sites from national immunization programs may also be considered.

For precautions to be taken before administering the vaccine, see section 4.4.

**4.3 Contraindications**

It is strictly prohibited to use this product under the following circumstances:

1. Individual has a history of allergic reaction to any component of the vaccine or similar vaccines.
2. Individual is suffering from the serious chronic diseases or allergic physique.
3. Individual who is suffering from fever or acute diseases shall postpone the vaccination of this vaccine.

**4.4 Special warnings and precautions for use**

1. Appropriate medical treatments, such as Adrenaline, should be readily available for immediate use in case of occasional severe anaphylactic reaction following vaccination. The recipients shall be observed for at least 30 minutes on site after injection.
2. This product should be used with caution in the following situations:

(1) People who has blood disorders such as a decrease in platelets (thrombocytopenia) or clotting disorders because of the risk of bleeding which may occur during intramuscular administration of the vaccine.

(2) People who is taking a treatment that suppresses the immune defenses or presenting with immune deficiency (immunosuppression). The immune response to the vaccine may be reduced. In such cases it is recommended to postpone vaccination until the end of the treatment or to make sure the subject is well protected. For patients with chronic immune deficiency, such as HIV infected individuals, it is recommended to administer this product even if the underlying disease may lead to limited immune response.

(3) Patients with uncontrolled epilepsy and other progressive neurological diseases.

3. As with any vaccine, a protective immune response may not be elicited in all recipients.

**4.5 Interaction with other medicinal products and other forms of interaction**

1. Currently, no clinical trial results have been provided for the combination of this product with other children's immunization schedule vaccines or non-immunization schedule vaccines.
2. Any drugs being taken or recently taken, including over-the-counter drugs, should be communicated with the physician.
3. This product should not be mixed with other drugs or vaccines in the same syringe for use.

**4.6 Undesirable effects**

Adverse reactions to this product are described below according to the frequency categories recommended by the Committee of International Organizations of Medical Sciences (CIOMS): very common (≥10%), common (1% to 10%, including 1%), uncommon (0.1% to 1%, including 0.1%), rare (0.01% to 0.1%, including 0.01%), and very rare (<0.01%):

**(1) Clinical Trials of This Product**

In the phase III clinical trials, 922 infants received at least one dose of this product, of them, 902 finished three-dose primary immunization and 822 further finished one booster dose at their 18 months old. Systematic safety observation was carried out within 7 days after each dose, and adverse events were collected through subjects' spontaneous report and investigators' regular follow-up within 8-30 days after each dose; meanwhile, serious adverse events were collected since the first dose until 30 days after the booster vaccination. Based on the safety data of phase III clinical trial, the adverse reactions of this product are described in accordance with Medical Dictionary for Regulatory Activities (MedDRA), are as follows:

*Systemic adverse reaction*

Common: Fever, irritability postvaccinal, diarrhea, vomiting, cough.

Uncommon: Recreased activity, dyspepsia, rhinorrhoea, productive cough, nasal obstruction, sneezing, decreased appetite, eczema, seizures, hypersensitivity, rash maculo-papular.

*Local adverse reaction*

Very common: Injection site erythema.

Common: Vaccination site swelling, tenderness, induration.

Uncommon: Vaccination site rash.

66.59% of the above adverse reactions were mild, and 33.00% were moderate. No serious adverse events related to this product were found. The adverse reactions of this product in booster immunization are basically consistent with the safety characteristics of primary immunization.

**(2) Clinical Trials of Preservative-free Single-dose sIPV**

In addition to the above adverse reactions, the following adverse reactions have been observed in clinical trials of preservative-free single-dose sIPV produced by the holder:

*Systemic adverse reaction*

Common: Nausea.

Uncommon: Crying, somnolence, pruritus, rash, Mucocutaneous rash, conjunctival hyperaemia.

*Local adverse reaction*

Uncommon: Vaccination site pruritus.

**(3) Clinical trials of similar products**

In addition to the above-mentioned adverse reactions, the following adverse reactions have also been observed in clinical trials of similar products:

1. Local reaction at the injection site: lymphadenopathy.
2. Systemic adverse reactions: eating disorder, hypersensitivity (urticaria, angioedema , anaphylactic shock ), joint pain and myalgia (moderate, transient), headache, paraesthesia (moderate, transient, mainly located in the lower limbs), excitation (disappears quickly within the first few hours or days after inoculation). Very early preterm infants (less than 28 weeks gestational age) may develop apnoea.

**(4) Post-marketing surveillance of similar products**

In addition to the above safety information, the following safety data (voluntarily reported by an uncertain population and cannot accurately assess its frequency or determine its association with vaccine use) were obtained by referring to post-marketing surveillance of similar products both domestically and internationally: Henoch-Schonlein purpura, thrombocytopenic purpura, abscess sterile, pigmentation, laryngeal edema, convulsions, etc.

**4.7 Overdose**

No overdose data have been obtained from clinical trials or literature reports yet.

**5. PHARMACOLOGICAL PROPERTIES**

**5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: Vaccine, viral vaccines

ATC code: J07BF03

**5.2 Clinical studies**

The phase III clinical trial of this product was conducted in two stages. The first stage was an open-label, single-arm safety observation in adults, children and infants with 24 subjects for each age group. The second stage was a randomized, blinded and controlled clinical trial. 1500 infants aged 2 months were randomly assigned into five groups, at a ratio of 1:1:1:1:1, namely test group 1, test group 2, test group 3, wIPV control group and single-dose sIPV control group. All subjects received 3 doses of test vaccines or control vaccines following the schedule of month 0, 1, 2 for the primary immunization, and one dose of test vaccines or control vaccines at 18 months of age for booster immunization. The per-protocol set (PPS) is the main analysis set for the immunogenicity evaluation. Based on PPS, the equivalence test among three batches of test vaccine and the non-inferiority test between the test vaccine group and the control group were carried out. The immunogenicity evaluation conclusions of full analysis set (FAS) and PPS are consistent.

**(1) Primary immunization**

The immunogenicity evaluation endpoints include the seroconversion rate and geometric mean titer (GMT) of neutralizing antibody at day 30 after the primary immunization. The seroconversion is defined as a change from seronegative (<1:8) to seropositive (≥1:8) or a 4-fold increase from baseline titers if seropositive. The serum antibody titer was determined using the World Health Organization standard method, i.e., micro-neutralization test method. The immunogenicity results of the primary immunization are shown in the following table:

Table 1 Seroconversion Rate of Neutralizing Antibody in Test Group Versus Control Groups at Day 30 After the Primary Immunization (PPS)

| Serotype | Seroconversion rate (n/N, %) | | | | | | Difference of seroconversion rate (95% CI) | |
|---|---|---|---|---|---|---|---|---|
| | Test group | | wIPV group | | Single-dose sIPV group | | Test group minuses wIPV group | Test group inuses single dose sIPV group |
| Type I | 794/810 | 98.02 | 268/277 | 96.75 | 265/271 | 97.79 | 1.28 (-1.02, 3.58) | 0.25 (-1.75, 2.24) |
| Type II | 762/810 | 94.07 | 240/277 | 86.64 | 252/271 | 92.99 | 7.42 (3.10, 11.74) | 1.08 (-2.37, 4.52) |
| Type III | 800/810 | 98.77 | 268/277 | 96.75 | 269/271 | 99.26 | 2.02 (-0.20, 4.24) | -0.50 (-1.77, 0.78) |

Note: The test group data are the combined results of the three batches of test vaccines.

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Table 2 Neutralizing Antibody Level of 30 Days After the Primary Vaccination (PPS) in Test and Control Group

| Serotype | Group | No. of analyzed subjects | Antibody level | | Antibody increase | |
|---|---|---|---|---|---|---|
| | | | GMT | 95%CI | GMI | 95%CI |
| Type I | Test group | 810 | 2717.0 | (2521.5, 2927.6) | 199.6 | (175.7, 226.7) |
| | wIPV group | 277 | 561.0 | (508.5, 619.0) | 47.5 | (40.5, 55.8) |
| | Single-dose sIPV group | 271 | 3027.5 | (2645.8, 3464.3) | 233.1 | (185.1, 293.5) |
| Type II | Test group | 810 | 459.7 | (433.1, 488.0) | 49.1 | (44.2, 54.6) |
| | wIPV group | 277 | 197.0 | (178.3, 217.6) | 21.0 | (17.6, 25.1) |
| | Single-dose sIPV group | 271 | 505.1 | (451.1, 565.7) | 52.6 | (43.2, 64.1) |
| Type III | Test group | 810 | 1998.2 | (1884.7, 2118.6) | 281.8 | (255.7, 310.7) |
| | wIPV group | 277 | 1044.1 | (937.3, 1163.1) | 129.2 | (107.7, 155.0) |
| | Single-dose sIPV group | 271 | 2215.4 | (2020.1, 2429.7) | 299.6 | (253.8, 353.7) |

Note: The test group data are the combined results of the three batches of test vaccines.

Table 3 Neutralizing Antibody Level of Different Test Groups at Day 30 After the Primary Immunization (PPS)

| Serotype | GMT (95% CI) | | | GMT ratio (95% CI) | | |
|---|---|---|---|---|---|---|
| | Test Group 1 (N=273) | Test Group 2 (N=274) | Test Group 3 (N=263) | Test Group 1 VS Test Group 2 | Test Group 1 VS Test Group 3 | Test Group 2 VS Test Group 3 |
| Type I | 2749.7 (2435.1, 3105.0) | 2965.9 (2604.0, 3378.1) | 2449.2 (2135.5, 2808.9) | 0.93 (0.78, 1.11) | 1.12 (0.94, 1.35) | 1.21 (1.00, 1.46) |
| Type II | 465.1 (420.9, 513.9) | 480.7 (434.0, 532.5) | 433.6 (388.8, 483.4) | 0.97 (0.84, 1.12) | 1.07 (0.93, 1.24) | 1.11 (0.96, 1.29) |
| Type III | 2119.6 (1922.4, 2337.1) | 2018.0 (1823.8, 2232.8) | 1860.4 (1673.6, 2068.2) | 1.05 (0.91, 1.21) | 1.14 (0.99, 1.32) | 1.08 (0.94, 1.26) |

**(2) Booster immunization (18 months old)**

This product conducted a booster immunization study on 2-month-old subjects in Phase III clinical trials at 18 months of age. The antibody status before booster immunization is shown in Table 4. The antibody level of the subjects after the booster immunization at 18 months of age is shown in Table 5.

Table 4 Immune Levels of Subjects 14 Months After Primary Immunization (Before Booster Immunization)

| Serotype | Group | No. of analyzed subjects | Seropositive rate | | Antibody level | |
|---|---|---|---|---|---|---|
| | | | N (%) | 95%CI | GMT | 95%CI |
| Type I | Test group | 858 | 858 (100.00) | (99.57, 100.00) | 642.57 | (593.51, 695.69) |
| | wIPV group | 290 | 290 (100.00) | (98.74, 100.00) | 193.05 | (169.94, 219.30) |
| | Single-dose sIPV group | 290 | 289 (99.66) | (98.09, 99.99) | 701.65 | (611.75, 804.77) |
| Type II | Test group | 858 | 857(99.88) | (99.35, 100.00) | 312.63 | (290.67, 336.25) |
| | wIPV group | 290 | 287(98.97) | (97.01, 99.79) | 142.34 | (124.43, 162.83) |
| | Single-dose sIPV group | 290 | 290(100.00) | (98.74, 100.00) | 327.51 | (287.52, 373.07) |
| Type III | Test group | 858 | 854(99.53) | (98.81, 99.87) | 325.81 | (300.15, 353.67) |
| | wIPV group | 290 | 284(97.23) | (95.55, 99.24) | 130.54 | (112.45, 151.53) |
| | Single-dose sIPV group | 290 | 289(99.66) | (98.09, 99.99) | 365.23 | (320.12, 416.69) |

Note: The test group data are the combined results of the three batches of test vaccines.

Table 5 Neutralizing Antibody Level of 30 Days After the Booster Vaccination in Trial and Control Group

| Serotype | Group | No. of analyzed subjects | Seroconversion rate | | Antibody level | | Antibody increase | |
|---|---|---|---|---|---|---|---|---|
| | | | % | 95%CI | GMT | 95%CI | GMI | 95%CI |
| Type I | Test group | 824 | 91.26 | (89.12, 93.10) | 9962.89 | (9530.88, 10414.49) | 15.76 | (14.54, 17.09) |
| | wIPV group | 278 | 92.45 | (88.68, 95.26) | 4086.46 | (3686.81, 4529.43) | 20.73 | (17.76, 24.20) |
| | Single-dose sIPV group | 285 | 89.47 | (85.31, 92.78) | 10202.27 | (9509.51, 10945.49) | 14.59 | (12.78, 16.67) |
| Type II | Test group | 824 | 97.82 | (96.57, 98.70) | 10273 | (9883.32, 10678.04) | 33.15 | (30.68, 35.82) |
| | wIPV group | 278 | 94.24 | (90.82, 96.67) | 4141.8 | (3728.04, 4601.49) | 29.03 | (24.87, 33.89) |
| | Single-dose sIPV group | 285 | 98.25 | (95.95, 99.43) | 10859.77 | (10230.53, 11527.72) | 33.19 | (29.13, 37.82) |
| Type III | Test group | 824 | 93.81 | (91.94, 95.36) | 7870.21 | (7507.80, 8250.10) | 24.5 | (22.44, 26.75) |
| | wIPV group | 278 | 96.4 | (93.48, 98.26) | 6844.97 | (6253.64, 7492.22) | 51.32 | (43.96, 59.92) |
| | Single-dose sIPV group | 285 | 92.28 | (88.55, 95.10) | 8046.47 | (7455.01, 8684.86) | 22.24 | (19.28, 25.64) |

Note: The test group data are the combined results of the three batches of test vaccines.

**6. PHARMACEUTICAL PARTICULARS**

**6.1 List of excipients**

Medium 199, glycine, sodium chloride, potassium chloride, calcium chloride, magnesium sulfate, disodium hydrogen phosphate, sodium dihydrogen phosphate and 2-phenoxyethanol.

**6.2 Shelf life**

The shelf life of the vaccine is 24 months.

**6.3 Special precautions for storage**

Store between +2°C and +8°C and protect from light.

Do not freeze.

After first opening, the vaccine can be used for up to 28 days provided it is stored between +2°C and +8°C.

Keep out of reach of children.

**6.4 Nature and contents of container**

2.5 mL suspension in a glass vial (type I glass) with a rubber stopper and a flip-off plastic cap with an aluminum seal. Each vial contains 5 doses.

**6.5 Special precautions for disposal and other handling**

*Handling instructions*

1. Do not use the vaccine if the vial has cracks, unclear or invalid label, abnormal color or foreign matters and the other abnormalities with its appearance, or the color of the vaccine vial monitor (VVM) in the central square is the same color as the ring or darker.
2. Special care should be taken to guarantee the injection does not enter a blood vessel.
3. After the first use, the product should be stored at a temperature between +2°C and +8°C and finished within 28 days. Before the second use, sterilize the surface of rubber stopper and avoid cross-contamination strictly. The error of inoculation volume caused by repeat extractions should be minimized. If less than 0.5 mL, the remaining vaccine should be discarded. The remaining vaccine from multiple vials must not be mixed for use.
4. The presentation of this product is 2.5 mL/vial containing 5 doses for human use, which shall be vaccinated according to the immunization dosage.

*Disposal*

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

**7. MANUFACTURER**

SINOVAC BIOTECH CO., LTD.

Registered address: No. 39, Shangdi Xi Road, Haidian District, Beijing, 100085, P. R. China.

Manufacturing address: No. 15, Zhi Tong Road, Changping Science Park, Changping District, Beijing, 102200, P. R. China.

Tel.: 400-898-2688

Fax: 86-10-62966910

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**8. DATE OF FIRST AUTHORISATION**

Date of First Authorization in China: 09 April 2024

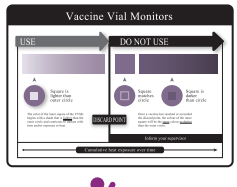
Date of First Authorized by WHO PQ Team:

**9. DATE OF REVISION OF THE TEXT**

Not applicable.

**10. VACCINE VIAL MONITOR**

Vaccine Vial Monitors (VVMs) are part of the label on Poliomyelitis Vaccine (Vero Cell), Inactivated, Sabin Strains supplied through Sinovac Biotech Co., Ltd. The color dot which appears on the label of the vial is a VVM. This 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 by observation of the color change progressively in the central square. As long as the colour of this square is lighter than the colour of the ring, 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, the vial should be discarded. VVM7 is used for Poliomyelitis Vaccine (Vero Cell), Inactivated, Sabin Strains and it may reach the endpoint for use before the vaccine reaches the end of the shelf life.

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