Date of Approval:
Date of Revision:

SINOVAC

Poliomyelitis Vaccine (Vero Cell), Inactivated, Sabin Strains

【NAME OF THE MEDICAL PRODUCT】
Poliomyelitis Vaccine (Vero Cell), Inactivated, Sabin Strains
【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. The color of the vaccine varies from colorless to light yellow.
The manufacturing and control of sIPV conforms to the current WHO requirements.
【COMPOSITION】
Suspension for injection in a 2 mL glass vial.
Each dose of 0.5 mL contains:
Active components:
Inactivated poliovirus Type 1, Sabin 15 D-antigen units
Inactivated poliovirus Type 2, Sabin 45 D-antigen units
Inactivated poliovirus Type 3, Sabin 45 D-antigen units
Excipients:
Medium 199, glycine, sodium chloride, potassium chloride, calcium chloride, magnesium sulfate, disodium hydrogen phosphate, and sodium dihydrogen phosphate.
【THERAPEUTIC INDICATION】
Poliomyelitis Vaccine (Vero Cell), Inactivated, Sabin Strains is indicated for active immunization of infants aged two months and above and children against Type 1, 2 and 3 polioviruses for the prevention of poliomyelitis caused by poliovirus Type 1, 2, and 3.
【ADMINISTRATION AND DOSAGE】
Poliomyelitis Vaccine (Vero Cell), Inactivated, Sabin Strains shall be administered by intramuscular injection. More specifically, it shall be administered in the middle anterolateral thigh for infants and deltoid for children. Recommendations about injection site from national immunization programs may also be considered. This vaccine is given to infants at 2-3-4 months of age as primary vaccination and a booster dose at 18 months of age.
【ADVERSE REACTIONS】
In phase I, II and III pre-licensure clinical trials, 739 infants were administered this product for three doses of primary vaccination, among which 541 infants in the phase III clinical trial completed one booster dose at the age of 18 months. Systematic safety follow-up observation was carried out within 7 days after each dose vaccination, and adverse events were collected through subjects' spontaneous reports and investigators' regular follow-up within 8-30 days after each dose; meanwhile, serious adverse events were collected within 0-30 days after vaccination in all the clinical trials, as well as the period from 30 days after the primary vaccination till 30 days after the booster vaccination in the phase III clinical trial.
According to the grading standard of adverse reaction incidence from the Council for International Organizations of Medical Sciences (CIOMS), i.e. very common (≥10%), common (≥1% and <10%), uncommon (≥0.1% and <1%), rare (≥0.01% and <0.1%) and very rare (<0.01%), the adverse reactions are classified as follows:
System adverse reaction
Very common: Fever (≥37.1°C) and diarrhea
Common: Nausea, vomiting, decreased appetite, and abnormal activity level
Uncommon: Hypersensitivity, crying, irritability, drowsiness, pruritus, rash, erythema, and conjunctival congestion
Local adverse reaction
Common: Redness, swelling, and induration
Uncommon: Pruritus and rash
Serious adverse reaction
63.64% adverse reactions above were mild and 35.33% were moderate. During the clinical trials, no serious adverse events related to this product occurred.
【SPECIAL WARNINGS AND PRECAUTIONS FOR USE】
1. Health-care providers should confirm with patients, parents, or guardians about reactions to a previous dose of this product or similar product.
2. 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.
3. Special care should be taken to guarantee the injection does not enter a blood vessel.
4. The vaccine should be administered with caution to people with blood disorders such as a decrease in platelets (thrombocytopenia) or clotting disorders since bleeding may occur following intramuscular administration of the vaccine.
5. People are taking a treatment that suppresses immune defenses (corticosteroid drugs, cytotoxic drugs, radiotherapy, or any other treatments likely to weaken immune defenses) or if patients present 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.
6. The vaccine does not contain preservatives. Therefore, it should be administered immediately after the container is opened.
7. Do not use the vaccine if the vial has cracks, unclear or invalid label, abnormal color or foreign matter, or the color of the vaccine vial monitor (VVM) in the central square is the same color as the ring or darker.
8. As with any vaccine, a protective immune response may not be elicited in all recipients.
【PREGNANCY AND LACTATION】
Although there is no evidence that sIPV has an adverse effect when administered to a pregnant woman or can affect reproduction capacity, it should be given to a pregnant woman only if it is clearly needed.
【CO-ADMINISTRATION WITH OTHER MEDICINAL PRODUCTS】
There is no known co-administration data of Poliomyelitis Vaccine (Vero Cell), Inactivated, Sabin Strains with other medicinal products.
【CONTRAINDICATIONS】
Poliomyelitis Vaccine (Vero Cell), Inactivated, Sabin Strains is contraindicated in persons with a history of allergic reaction to any component of the vaccine or similar vaccines or suffering from acute diseases, serious chronic diseases, acute attack of the chronic diseases, fever, uncontrolled epilepsy or other ongoing nervous system diseases.
【CLINICAL STUDIES】
This product has completed phase I, phase II, phase III pivotal clinical trials, and phase III sIPV & OPV sequential vaccination clinical trials, as well as the cross-neutralization study based on the serum collected in the phase II clinical trial.

Table 1 Summary of the Pre-Licensure Clinical Trials

Phase	Study design	Number of subjects	Population
Phase II	Randomized, blinded, double parallel and controlled clinical trial including low dose group, middle dose group and high dose group of experimental groups, wIPV control group and sIPV control group	600 subjects in total and 120 subjects for each group	Infants aged 2 months
Phase III (all-IPV)	Primary vaccination: randomized, blinded, positive control (wIPV) and non-inferiority; Booster vaccination: open, positive control (wIPV)	Primary vaccination: 599 subjects in the experimental group and 600 subjects in the control group. Booster vaccination: 541 subjects in the experimental group and 544 subjects in the control group.	Infants aged 2 months
Phase III (sIPV & bOPV)	Randomized, positive control, non-inferiority	120 subjects for each schedule of "sIPV+2bOPV" and "2sIPV+bOPV"	Infants aged 2 months

Primary Vaccination
In the phase III pivotal clinical trial, the immunogenicity endpoint evaluation and non-inferiority analysis were conducted based on the per-protocol set (PPS). A total of 553 subjects in the experimental group and 652 subjects in the control group were included in the PPS. The clinical trial results of FAS and PPS are consistent.
The immunogenicity evaluation endpoints include the seroconversion rates and geometric mean titer (GMT). 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 assay was performed using the World Health Organization standard method, i.e. micro-neutralization test method. The immunogenicity results of the primary vaccination are shown in Table 2 and Table 3.

Table 2 Seroconversion Rate of Neutralizing Antibody 30 Days after the Primary Vaccination (PPS*)

Type	sIPV		wIPV		sIPV group minus wIPV group
	n/N	%	n/N	%	Difference% (95% CI)
Type 1	542/553	98.01	529/562	94.13	3.88 (1.62, 6.15)
Type 2	524/553	94.76	472/562	83.99	10.77 (7.21, 14.33)
Type 3	547/553	98.92	549/562	97.69	1.23 (-0.29, 2.74)

*PPS: Per Protocol Set, same as below.

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Table 3 Neutralizing Antibody Level 30 Days after the Primary Vaccination (PPS)

Type/Group		Number of subjects	Average antibody level		Average antibody increase	
			GMT	95% CI	GMR	95% CI
Type 1	sIPV	553	4,149.72	(3,828.3, 4,498.1)	307.88	(264.44, 358.45)
	wIPV	562	493.49	(459.53, 529.97)	34.52	(30.61, 38.92)
Type 2	sIPV	553	392.42	(362.51, 424.79)	42.65	(37.51, 48.50)
	wIPV	562	158.75	(146.93, 171.52)	16.22	(14.22, 18.50)
Type 3	sIPV	553	1,372.34	(1,281.4, 1,469.7)	231.53	(208.08, 257.62)
	wIPV	562	550.80	(509.29, 595.69)	90.92	(81.36, 101.61)

Booster vaccination
The booster dose was administered to the subjects of the phase III pivotal clinical trial at the age of 18 months and the immunogenicity data before and after the booster vaccination are shown in Table 4 and Table 5, respectively.

Table 4 Immunogenicity Data 14 Months after the Primary Vaccination (Before the Booster Vaccination)

Type/Group		Number of subjects	Seropositive rate（1:8）		Average antibody level	
			n (%)	95% CI	GMT	95% CI
Type 1	sIPV	540	538 (99.63)	(98.67, 99.96)	750.52	(681.03, 827.09)
	wIPV	542	539 (99.45)	(98.39, 99.89)	177.42	(161.46, 194.96)
Type 2	sIPV	540	532 (98.52)	(97.10, 99.36)	108.36	(98.96, 118.64)
	wIPV	542	517 (95.39)	(93.27, 96.99)	50.82	(46.31, 55.76)
Type 3	sIPV	540	540 (100.0)	(99.32, 100.0)	411.68	(373.43, 453.85)
	wIPV	542	530 (97.79)	(96.16, 98.85)	154.03	(135.69, 174.86)

Table 5 Immunogenicity Data 30 Days after the Booster Vaccination

Type/Group		Number of subjects	Seroconversion rate		Average antibody level		Average antibody increase (Compared with pre-booster dose)	
			n%	95% CI	GMT	95% CI	GMR	95% CI
Type 1	sIPV	413	378 (91.53)	(88.41, 94.03)	11,176.75	(10,588, 11,799)	15.07	(13.58, 16.73)
	wIPV	409	382 (93.40)	(90.54, 95.60)	4,524.23	(4,194.8, 4,879.5)	24.67	(21.80, 27.92)
Type 2	sIPV	413	406 (98.31)	(96.54, 99.32)	4,871.22	(4,494.3, 5,279.8)	46.16	(41.10, 51.85)
	wIPV	409	394 (96.33)	(94.02, 97.93)	2,057.89	(1,888.5, 2,242.5)	38.88	(34.15, 44.26)
Type 3	sIPV	413	388 (93.95)	(91.19, 96.04)	10,907.19	(10,347, 11,498)	26.69	(23.66, 30.11)
	wIPV	409	386 (94.38)	(91.68, 96.40)	7,538.18	(6,962.9, 8,161.0)	48.33	(41.64, 56.09)

Cross neutralization study
Pre-vaccination and post-vaccination paired backup serum of 250 subjects from five parallel groups (50 in each group) in the phase II clinical trial were used for the cross-neutralization study (10 poliovirus strains), including 4 type 1 strains (Sabin cVDPV1, and imported type 1 wild strain in China in 2011), 3 type 2 strains (Sabin 2, MEF-1, and cVDPV2), and 3 type 3 strains (Sabin 3, Saukett, and cVDPV3). The immunogenicity results calculated based on PPS are listed as follows:
The post-vaccination seropositive rates against all strains of type 1 were 100%; the seroconversion rates were 91%-100%, and the GMTs were 48-1,303. The seropositive rates against all strains of type 2 were 98%-100%; the seroconversion rates were 96%-100% and the GMTs were 209-336. The seropositive rates against all strains of type 3 were 100%; seroconversion rates were 98%-100% and GMTs were 486-647.
Sequential vaccination study
The immunogenicity data of the sequential vaccination study is shown in Table 6, Table 7, Table 8 and Table 9.

Table 6 Seroconversion Rate of Neutralizing Antibody 30 Days after sIPV+2bOPV Schedule (PPS)

Type	sIPV+2bOPV		wIPV+2bOPV		sIPV group minus wIPV group
	n/N	%	n/N	%	Difference% (95% CI)
Type 1	106/107	99.07	109/110	99.09	-0.03 (-2.57, 2.52)
Type 2	58/107	54.21	57/110	51.82	2.39 (-10.89, 15.67)
Type 3	105/107	98.13	110/110	100	-1.87 (-4.44, 0.70)

Table 7 Neutralizing Antibody Level and GMR 30 Days after sIPV+2bOPV Schedule (PPS)

Type/Group		Number of subjects	Average antibody level		Average antibody increase	
			GMT	95% CI	GMR	95% CI
Type 1	sIPV+2bOPV	107	5,761.22	(4,847.5, 6,847.2)	437.63	(321.44, 595.83)
	wIPV+2bOPV	110	3,196.76	(2,745.8, 3,721.7)	259.99	(194.79, 347.02)
Type 2	sIPV+2bOPV	107	27.70	(21.61, 35.52)	2.71	(1.97, 3.73)
	wIPV+2bOPV	110	21.94	(17.97, 26.77)	2.16	(1.59, 2.91)
Type 3	sIPV+2bOPV	107	2,074.75	(1,700.3, 2,531.6)	321.27	(239.17, 431.56)
	wIPV+2bOPV	110	2,097.07	(1,791.1, 2,455.4)	333.89	(264.95, 420.75)

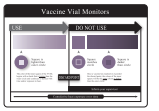
Table 8 Seroconversion Rate of Neutralizing Antibody 30 Days after 2sIPV+bOPV Schedule (PPS)

Type	2sIPV+bOPV		2wIPV+bOPV		sIPV group minus wIPV group
	n/N	%	n/N	%	Difference% (95% CI)
Type 1	117/118	99.15	110/110	100	-0.85 (-2.50, 0.81)
Type 2	96/118	81.36	82/110	74.55	6.81 (-3.94, 17.56)
Type 3	116/118	98.31	110/110	100	-1.69 (-4.02, 0.63)

Table 9 Neutralizing Antibody level and GMR 30 Days after 2sIPV+bOPV Schedule (PPS)

Type/Group		Number of subjects	Average antibody level		Average antibody increase	
			GMT	95% CI	GMR	95% CI
Type 1	2sIPV+bOPV	118	10,119.23	(8,464, 12,098)	830.86	(619.8, 1,113.8)
	2wIPV+bOPV	110	5,801.69	(4,848.1, 6,942.8)	453.37	(333.67, 616.02)
Type 2	2sIPV+bOPV	118	133.91	(108.72, 164.93)	16.17	(11.85, 22.06)
	2wIPV+bOPV	110	84.24	(69.20, 102.55)	10.30	(7.77, 13.65)
Type 3	2sIPV+bOPV	118	7,255.10	(6,093.8, 8,637.7)	1,108.83	(870.3, 1,412.8)
	2wIPV+bOPV	110	6,124.20	(4,939.9, 7,592.4)	984.85	(769.9, 1,259.8)

【OVERDOSING】No cases of overdosing have been reported.
【VACCINE PRESENTATIONS】Glass vial containing one dose (0.5 mL) of Poliomyelitis Vaccine (Vero Cell), Inactivated, Sabin Strains (sIPV).
【STORAGE】The vaccine is stable if stored at temperature between +2°C and +8°C. Do not freeze.
【SHELF LIFE】The shelf life of the vaccine is 24 months.
The vaccine satisfies the recommendations given by the World Health Organization in WHO TRS No. 993, Annex 3, 2015, and Pharmacopoeia of the People's Republic of China (Edition 2020).
【THE 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 real-time temperature sensor 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 color of this square is lighter than the color of the ring, the vaccine can be used. As soon as the color of the central square is the same color as the ring or of a darker color 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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