Summary of Product Characteristics

Poliomyelitis Vaccine (Vero Cell), Inactivated, Sabin Strains

1. Qualitative and Quantitative Composition

1.1 Strength

0.5mL/dose/vial.

Each dose (0.5mL) contains:

Active Composition: Poliovirus (inactivated) Type I (Sabin) 15DU

Poliovirus (inactivated) Type II (Sabin) 45DU

Poliovirus (inactivated) Type III (Sabin) 45DU

Excipients: M199 media (containing amino acids, mineral salts, vitamins, glucose, etc.), sodium hydroxide used for pH adjustment.

The Poliomyelitis Vaccine (Vero Cell), Inactivated, Sabin Strains is formulated with Type I, Type II and Type III Sabin strains which are inoculated respectively on the Vero cell for culturing, virus harvesting, concentration, purification and formaldehyde-inactivation, then mixing together to form the trivalent liquid vaccine. This vaccine complies with WHO's recommendations.

1.2 Pharmaceutical form

Liquid Injection

This product is a clear, transparent, object-free and colorless liquid.

2. Clinical Particulars

2.1 Therapeutic Indication

This product is indicated for the prevention of poliomyelitis in infants from 2 months and toddlers aged 18 months.

2.2 Posology and Method of Administration

This vaccine will be administered by a healthcare professional, preferably into a muscle (intramuscular route). This injection into a muscle will be preferably performed in the middle of the outer thigh in infants and in the upper part of the arm in toddlers.

For primary vaccination (first series of vaccination), the first one dose should be injected at the age of 2 months, then two successive doses at an interval of 4-6 weeks. One dose should be injected as a booster at the age of 18 months.

This vaccine should be used immediately once open.

The immune persistency study of this vaccine has not been conducted.

2.3 Contraindication

The vaccine is strictly prohibited in the following cases:

Individuals who are allergic to any component (active, excipients) of this product, or those who have allergic reactions with vaccines before.

Individuals who have serious chronic diseases or history of hypersensitivity.

Vaccination should be postponed if individuals have fever or during the acute phase of disease.

2.4 Special Warning and Precaution for Use

1) Intravascular injection is strictly prohibited.
2) Drugs and equipment such as epinephrine should be available for emergency treatment in the event of an occasional severe allergic reaction. The vaccinee should be observed for at least 30 minutes after vaccination.
3) This vaccine should be used with caution if:
   a) have blood disorders such as decrease in platelets (thrombocytopenia) or clotting disorders because of the risk of bleeding which may occur during intramuscular administration of this vaccine.
   b) are taking a treatment that suppresses your immune defence or if you present with immune deficiency, 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. If you have chronic immune deficiency, this vaccine may also be recommended even though the underlying disease may cause a limited immune response.
   c) have uncontrolled epilepsy and other progressive neurological disorders.
4) Like all vaccines, this product may not have 100% preventive effect for vaccinee.
5) Do not use disinfectant to contact the vaccine when vial opening and injection.

6) This vaccine should be used immediately after open.
7) Do not use after the expiration date stated on the box and on the label.
8) Do not use if the product has a cloudy appearance or the vial has cracks.
9) Keep away from reach of children.

2.5 Interaction with Other Medicinal Products and Other Forms of Interaction

If any drugs, including over-the-counter drugs, are being taken or recently taken, please inform the physician in time.

This IPV vaccine and DTaP vaccine can be co-administered. There is no immunogenicity and safety data on co-administration with other vaccines other than DTaP.

2.6 Fertility, Pregnancy and Breastfeeding

The relevant research has not been carried out in Fertility, Pregnancy and Breastfeeding

2.7 Effect on Ability to Drive and Machine

N/A

2.8 Undesirable Effects

a. Summary of the safety profile

According to the adverse reactions (ARs) of this vaccine reported in domestic clinical trial, the incidence for ARs (CIOMS recommendation) can be presented as: Very common (≥10%), common (1-10%, including 1%), uncommon (0.1-1%, including 0.1%), rare (0.01-0.1%, including 0.01%) and very rare (< 0.01%), and detailed ARs are described as follows.

Very Common:

- Fever (moderate, transiently).

Common:

- ARs at the Injection Site: Pain, redness.
- Systemic ARs: Agitation, vomiting, somnolence, eating disorder, diarrhea.

Uncommon:

- ARs at the Injection Site: Induration.
- Systemic ARs: Rash.

Very Rare (Refer to the marketed similar vaccines):

- ARs at the Injection Site: Lymph nodes enlarged.

- Allergic Reactions Caused by Any Component of Vaccine: Urticaria, angioedema, anaphylactic shock.
- May occur moderate, transient arthralgia and myalgia.
- May occur convulsions (with or without fever).
- May occur headache, moderate and transient paresthesia (mainly in the lower limbs) within two weeks after vaccination.
- May occur excitation within the first few hours or days after vaccination, but will soon disappear spontaneously.
- Widespread rash.

b. Tabulated summary of adverse reactions

Adverse reactions	Symptoms
Very common	Fever (moderate, transiently)
Common	Pain, redness at the injection site; Agitation, vomiting, somnolence, eating disorder, diarrhea.
Uncommon	Induration at the injection site; Rash
Very rare	Lymph nodes enlarged at the injection site; Allergic reactions caused by any component of vaccine: Urticaria, angioedema, anaphylactic shock. May occur moderate, transient arthralgia and myalgia. May occur convulsions (with or without fever). May occur headache, moderate and transient paresthesia (mainly in the lower limbs) within two weeks after vaccination. May occur excitation within the first few hours or days after vaccination, but will soon disappear spontaneously. Widespread rash.

c. Description of selected adverse reactions

All participants were observed for immediate reaction 30 minutes after each vaccination by the investigators. During Day 0-7 after each vaccination, active observation for system safety was carried out, and the participants or his/her legal guardian were asked to record the adverse events and medication usage on a diary card. During Day 8-30 after each vaccination, information on occurrence of adverse events was collected through the combination of telephone active follow-up visit and active report of subjects, and recorded on a contact card by participants or his/her legal guardian.

This allowed recording of these assessments only within a fixed time window and provided an

accurate representation of the participant's experience at that time. Participants were asked to assess local reactions and systemic events.

The solicited local reactions included tenderness, redness, swelling and sclerosis at the injection site.

The solicited systemic reactions included fever, irritability (abnormal crying), vomiting, lactation or eating disorders, lethargy, convulsion, allergic reaction.

d. Pediatric population

This product is indicated for the prevention of poliomyelitis in infants from 2 months and toddlers, so the information in 4.8 Undesirable Effects is applicable for Pediatric population.

e. Other special population(s)

N/A

2.9 Overdose

N/A

Submit adverse reactions reports to:

PT Jakarta Biopharmaceutical Industry

Jl. Musi no. 15, Cideng, Kec. Gambir, Jakarta Pusat 10150

Email: admin@jbio.co.id Tel: +62-21-50208838

3. Pharmacological Properties

3.1 Pharmacodynamics Properties

a. Pharmacotherapeutic Group and ATC Code:

J07BF03

b. Mechanism of Action (if known)

The antibodies against poliovirus can be produced after vaccination, to prevent poliomyelitis caused by Type I, Type II and Type III poliovirus.

c. Pharmacodynamic Effects.

Refer to "d. Clinical Efficacy and Safety"

d. Clinical Efficacy and Safety

According to WHO Technical Report Series No. 993, 2015 Part C.1, due to the dramatic decrease of poliomyelitis cases after the establishment of the GPEI following the 1998 World Health Assembly resolution, clinical efficacy studies to support the licensure of a candidate IPV are no longer feasible. Thus, a non-inferiority study in terms of immunogenicity against already licensed vaccine wIPV (Sanofi Pasteur) have been conducted. The immunogenicity results are as follows.

Totally 1,200 subjects aged 2 months were included in the phase III clinical trial of Poliomyelitis Vaccine (Vero Cell), Inactivated, Sabin Strains from Beijing Institute of Biological Products Co., Ltd., and among whom, 1,173 (97.75%) completed the primary immunization. All the 1,200 subjects entered into the safety analysis set and full analysis set (FAS), and among whom, 1,164 (97.0%) entered the per-protocol analysis set (PPS), and 27 (2.25%) were dropouts. The compliance of the subjects met the requirements of the protocol. The conclusions of immunogenicity and safety are following:

Immunogenicity:

(1) After primary immunization, in the trial group, the seroconversion (4-fold increase) rates of neutralizing antibodies Type I, II and III poliovirus in the total population, the seroconversion rate in the antibody-negative population before vaccination and the 4-fold increase rates in the antibody-positive population before vaccination were not inferior to the control group. Type I, II and III antibodies against poliovirus in all subjects in the trial group were ≥1:8; with an antibody positive rate of 100%, and the antibody positive rate with a neutralizing antibody titer of ≥1:64 reached above 97%.

(2) After primary immunization, the seroconversion rates of antibody against Type I, II and III poliovirus with a boundary value of ≥1:8 in the antibody-negative population before vaccination was 100% in the trial group and the control group, with no significant difference between the groups; for the seroconversion rate of antibody with a boundary value of ≥1:64, there was no difference between groups for Type I and Type III, and the trial group was higher than the control group for Type II.

(3) After primary immunization, the 4-fold increase rate and the rate of titer ≥ 1:64 in the antibody-positive population before vaccination was higher in the trial group than those in the control group for Type I and II, after correcting the antibodies before immunization, the 4-fold increase rates of antibodies against Type I, II and III poliovirus in each group were no less than 90%, showing no significant difference between the groups in 4-fold increase rates of antibodies against Type I and Type III; the 4-fold increase rate of antibodies against Type II in the trial group was higher than that in the control group.

(4) After primary immunization, the GMT and antibody fold increase of neutralizing antibodies against Type I, II and III poliovirus in the trial group were significantly higher than those in the control group.

Table 1 Antibody GMT Before and After Primary Immunization and Antibody Fold Increase

Group		Trial Group				Control Group			
		No. of Analysis	GMT Before Immunization	GMT after Immunization	Increasing Multiple	No. of Analysis	GMT Before Immunization	GMT after Immunization	Increasing Multiple
PPS	Type I	583	17.31	4930.67	284.80	581	18.38	588.64	32.02
	Type II		8.90	554.15	62.27		8.47	163.98	19.37
	Type III		6.92	1397.96	202.15		6.44	655.42	101.83
FAS	Type I	600	17.47	4399.70	251.80	600	18.53	542.20	29.27
	Type II		8.95	511.34	57.12		8.60	153.62	17.86
	Type III		6.87	1233.56	179.55		6.43	583.85	90.79

Reference: Phase III CSR table 16, table 29, table 30

(5) The comprehensive analysis of seroconversion rate and antibody level of the same group in phase II and phase III clinical trials shows that the seroconversion rates of poliovirus Type I, II and III antibodies in the trial group in phase III clinical trial and the middle dosage group in phase II clinical trial were 100% for those with negative antibodies before immunization; the level of antibodies against Type I and Type III poliovirus of the trial group and control group in phase III clinical trial group was higher than that in the phase II clinical trial. The GMT and fold increase of Type II antibodies in phase II and III clinical trials were similar to each other; after maternal transferred antibodies correction for those with positivity antibodies before immunization, the seroconversion (4-fold increase) rates of Type I, II and III antibodies against poliovirus were greater than 95% in phase II and III clinical trials; in phase III clinical trial, the seroconversion (4-fold increase) rate of Type II antibodies of the trial group was higher than that of the control group.

Table 2 Seroconversion Rate and Antibody Level in Antibody-negative Population before vaccination in Phase II and Phase III Clinical Trials

Group			Observation Number	Seroconversion (4-fold increase) %	GMT	Increasing Multiple
Type I	Phase II	Middle dose group	38	100.0	3873.95	968.49
		wIPV control	36	100.0	484.33	121.08
	Phase III	Trial group	181	100.0	7502.49	1875.62
		Control group	173	100.0	594.59	148.65
Type II	Phase II	Middle dose group	56	100.0	623.28	155.82
		wIPV control	64	100.0	204.97	51.24

	Phase III	Trial group	302	100.0	758.24	189.56
		Control group	311	100.0	203.65	50.91
Type III	Phase II	Middle dose group	72	100.0	1036.18	259.05
		wIPV control	78	100.0	513.82	128.45
	Phase III	Trial group	396	100.0	1604.99	401.25
		Control group	410	100.0	705.38	176.34

Reference: Phase III CSR table 50, table 51, table 52

Table 3 Corrected Seroconversion (4-fold increase) Rate of Population with Negative Antibodies before Immunization in Phase II and Phase III Clinical Trials

Group		Trial Group		Control Group	
		Analysis Number	Seroconversion (4-fold increase) %	Analysis Number	Seroconversion (4-fold increase) %
Phase II	Type I	98	100.0	95	98.95
	Type II		100.0		100.0
	Type III		100.0		100.0
Phase III	Type I	583	98.46	581	97.76
	Type II		99.14		96.90
	Type III		99.66		99.83

Reference: Phase III CSR table 60

3.2 Pharmacokinetics Properties

N/A

3.3 Preclinical Safety Data

In immunogenicity study, the sIPV showed good immunogenicity after immunization with Wistar rats.

In the muscle irritation study on New Zealand rabbits, animals were intramuscularly injected once by self-control method on D1, D4, D7, D10 and D13 respectively (a total of 5 times), with the dosing volume of 0.5 mL/animal, i.e. 1 dose/animal (each dose contained 15 DU of Type I poliovirus antigen, 45 DU of Type II poliovirus antigen and 45 DU of Type III poliovirus antigen). After intramuscular injection of Poliomyelitis Vaccine (Vero Cell), Inactivated, Sabin Strains, no irritation related to the action of the test article was observed.

In active systemic anaphylaxis study on guinea pigs, animals were sensitized by intramuscular injection of the sIPV at a dose of 0.1 dose/animal and 1 dose/animal, respectively (a total of 3 times),

and excited by intravenous injection at a dose of 0.2 dose/animal and 2 doses/animal, respectively. The active systemic anaphylaxis was negative in guinea pigs.

4. Pharmaceutical Particulars

4.1 List of Excipients

M199 media (containing amino acids, mineral salts, vitamins, glucose, etc.), sodium hydroxide.

4.2 Incompatibilities

The container-content compatibility study is essential to guarantee the quality of the vaccine product in contact with designated materials. BIBP has performed the container-content compatibility studies to demonstrate whether the material has an impact on product quality. The studies indicate that no elements and organic matter exceed the limit, no erosion is observed on the inner surface of the glass in the 25±2℃ for 60-day, in 37±2℃ for 11-day, and 30-month long-term leachable study.

4.3 Shelf Life

24 months

4.4 Special Precaution for Storage

Store and transport in a refrigerated (2℃-8℃) condition, protect from light. Do not freeze.

4.5 Nature and Content of Container

This is a liquid vaccine, and the primary packaging is a vial.

Packaging: Box, 1 vial @ 0.5 mL

Box, 10 vials @ 0,5 mL

Film-coated middle-borosilicate glass vial is a kind of simple structured, unbreakable, and low cost material which is comprehensively used for vaccine product. The vial is composed of film-coated middle-borosilicate glass vial, aluminum foil cap and film-coated rubber stopper.

4.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

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

5. Manufacturer

Name: Beijing Institute of Biological Products Co., Ltd.

Manufacturing Address: No. 6&9 Bo'xing 2nd Road, Economic-Technological Development Area, Beijing, P.R. China

6. Marketing Authorization Holder

Name: PT. Jakarta Biopharmaceutical Industry

Address: Kawasan Industri Modern Cikande Jalan Modern Industri XV Blok AD No. 3, Desa Sukatani, Indonesia

7. Marketing Authorization Number

Registration No. :

Date of first approval:

INFORMASI PRODUK UNTUK PASIEN

POLIOMYELITIS VACCINE (VERO CELL), INACTIVATED, SABIN STRAINS

1. BENTUK SEDIAAN

Cairan Injeksi

2. PEMERIAN OBAT

Cairan bening, transparan, bebas objek, dan tidak berwarna

3. KOMPOSISI ZAT AKTIF DAN KEKUATAN OBAT

Setiap dosis (0,5 mL) mengandung:

- Poliovirus (inactivated) Type I (Sabin) 15 DU
- Poliovirus (inactivated) Type II (Sabin) 45 DU
- Poliovirus (inactivated) Type III (Sabin) 45 DU

4. INDIKASI

Produk ini diindikasikan untuk pencegahan poliomyelitis pada bayi dari usia 2 bulan dan balita usia 18 bulan.

5. POSOLOGI DAN CARA PEMBERIAN

Vaksin ini disuntikkan ke dalam otot (intramuskular). Suntikan ke dalam otot ini sebaiknya dilakukan di tengah paha luar pada bayi, dan di bagian atas lengan pada balita.

Untuk vaksinasi primer, satu dosis pertama harus disuntikkan pada usia 2 bulan, kemudian dua dosis berturut-turut pada interval 4-6 minggu. Satu dosis harus disuntikkan sebagai *booster* pada usia 18 bulan.

6. KONTRAINDIKASI

Vaksin ini sangat dilarang dalam kasus-kasus berikut:

a. Individu yang alergi terhadap komponen apa pun (aktif, eksipien) dari produk ini, atau mereka yang memiliki reaksi alergi pada vaksin-vaksin sebelumnya
b. Individu yang memiliki penyakit kronis serius atau riwayat hipersensitivitas
c. Vaksinasi harus ditunda jika individu mengalami demam atau dalam fase akut penyakit

7. PERINGATAN DAN PERHATIAN

a. Injeksi intravaskular sangat dilarang
b. Obat-obatan dan peralatan seperti epinefrin harus tersedia untuk perawatan darurat jika terjadi reaksi alergi berat. Pasien harus diamati setidaknya selama 30 menit setelah divaksinasi
c. Vaksin ini harus digunakan dengan hati-hati jika:
    i. memiliki kelainan darah seperti penurunan trombosit (trombositopenia) atau gangguan pembekuan karena risiko perdarahan yang mungkin terjadi selama pemberian vaksin ini secara intramuskuler.
    ii. mengambil pengobatan yang menekan pertahanan imun Anda atau jika Anda hadir dengan defisiensi imun, respons imun terhadap vaksin dapat berkurang. Dalam kasus seperti ini, disarankan untuk menunda vaksinasi sampai akhir perawatan atau untuk

memastikan subjek terlindungi dengan baik. Jika Anda memiliki defisiensi imun kronis, vaksin ini juga dapat direkomendasikan meskipun penyakit yang mendasarinya dapat menyebabkan respons imun yang terbatas.

iii. memiliki epilepsi yang tidak terkontrol dan gangguan neurologis progresif lainnya.

d. Seperti semua vaksin, produk ini mungkin tidak memiliki efek pencegahan 100% untuk pasien
e. Jangan gunakan disinfektan untuk berkontak vaksin saat pembukaan botol dan injeksi
f. Vaksin ini harus digunakan lansung setelah dibuka
g. Jangan gunakan setelah tanggal kadaluwarsa yang tercantum pada dus dan label
h. Jangan gunakan jika produk mempunyai tampilan keruh atau botol retak
i. Jauhkan dari jangkauan anak-anak

8. INTERAKSI OBAT

Jika ada obat, termasuk obat bebas, sedang diminum atau baru-baru ini diminum, harap beri tahu petugas Kesehatan.

Vaksin IPV dan DTaP dapat diberikan bersamaan. Tidak ada data imunogenisitas dan keamanan penggunaan bersama dengan vaksin selain DTaP.

9. KEHAMILAN DAN MENYUSUI

Penelitian yang relevan belum dilakukan dalam Kesuburan, Kehamilan dan Menyusui.

10. EFEK SAMPING

Produk ini diindikasikan untuk pencegahan polio pada bayi mulai usia 2 bulan dan balita usia 18 bulan, sehingga informasi ini berlaku untuk populasi anak-anak.

a. Ringkasan tabulasi dari reaksi efek samping

Efek Samping	Gejala
Sangat Umum	Demam (sedang, sementara)
Umum	Nyeri, kemerahan di tempat suntikan; Agitasi, muntah, mengantuk, gangguan makan, diare.
Jarang	Indurasi di tempat injeksi; Ruam
Sangat Jarang	Kelenjar getah bening membesar di tempat injeksi; Reaksi alergi yang disebabkan oleh komponen vaksin apa pun: Urtikaria, angioedema, syok anafilaksis. Dapat terjadi arthralgia dan mialgia sedang, transien. Dapat terjadi kejang (dengan atau tanpa demam). Dapat terjadi sakit kepala, parestesia sedang dan sementara (terutama di tungkai bawah) dalam waktu dua minggu setelah vaksinasi. Dapat terjadi eksitasi dalam beberapa jam atau hari pertama setelah vaksinasi, tetapi akan segera menghilang secara spontan. Ruam meluas.

b. Deskripsi Reaksi Efek Samping

Semua peserta diamati untuk reaksi segera 30 menit setelah setiap vaksinasi oleh para peneliti. Selama Hari ke 0-7 setelah setiap vaksinasi, observasi aktif untuk keamanan sistem dilakukan, dan peserta atau wali sahnya diminta untuk mencatat efek samping dan penggunaan obat pada kartu

harian. Selama Hari ke 8-30 setelah setiap vaksinasi, informasi tentang terjadinya efek samping dikumpulkan melalui kombinasi kunjungan tindak lanjut aktif melalui telepon dan laporan aktif subjek, dan dicatat pada kartu kontak oleh peserta atau wali sahnya

Laporkan efek samping kepada:

PT Jakarta Biopharmaceutical Industry

Jl. Musi no. 15, Cideng, Kec. Gambir, Jakarta Pusat 10150

Email : admin@jbio.co.id

Tel: +62-21-50208838

11. KEMASAN

Dus, 1 vial @ 0,5 mL
Dus, 10 vial @ 0,5 mL

12. CARA PENYIMPANAN

Vaksin ini disimpan pada suhu +2 - +8°C, terlindungi dari cahaya. Vaksin ini tidak boleh dibekukan.

HARUS DENGAN RESEP DOKTER

13. NOMOR IJIN EDAR

Tanggal persetujuan pertama kali:

14. PRODUSEN

Beijing Institute of Biological Products Co., Ltd., Beijing, China

15. PENDAFTAR

PT Jakarta Biopharmaceutical Industry, Jakarta, Indonesia

HARUS DENGAN RESEP DOKTER