Poliomyelitis Vaccine (Oral) Bivalent Type 1 and 3

1. NAME OF THE MEDICINAL PRODUCT
Poliomyelitis Vaccine (Oral) Bivalent Type 1 and 3

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Poliomyelitis Vaccine (Oral) Bivalent Type 1 and 3 (bOPV) is a live attenuated poliomyelitis virus contains the sabin strains of Type 1 (LSc2ab-KP_2) and Type 3 (Leon 12, a1b-KP_3). The attenuated virus particles in bOPV are harvested from vero cell culture. 1 Molar Magnesium chloride is used as a stabilizer and also contains polysorbate 80. Poliomyelitis Vaccine is manufactured from the bulk imported from Bilthoven Biologicals B.V., Bilthoven, The Netherlands.

Each dose of 2 drops (0.1 ml) contains

Name of the Active Ingredients	Quantity per 0.1 ml [Each dose of 2 drops]
Polio virus (Sabin) Type 1*	$\geq 10^{6.0}$ $CCID_{50}$
Polio virus (Sabin) Type 3*	$\geq 10^{5.8}$ $CCID_{50}$

* Grown on Vero cell Culture.

$CCID_{50}$: Cell Culture Infectious Dose 50 %.

For the full list of excipients, see section 8.1.

3. PHARMACEUTICAL FORM AND STRENGTH
The vaccine is a light yellow to dark pink clear liquid in clear glass vial for oral administration.

Each dose of 0.1 ml (2 drops) contains not less than $10^{6.0}$ $CCID_{50}$ of Type 1 and not less than $10^{5.8}$ $CCID_{50}$ of Type 3 of live attenuated poliomyelitis virus of sabin strains.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications
Poliomyelitis Vaccine (Oral) Bivalent Type 1 and 3 is indicated for active immunization against infection caused by Type 1 and 3 Polioviruses.

4.2 Posology and Method of Administration
Posology:

One immunizing dose (0.1 ml) is contained in two drops in a multidose container.

The advised vaccination schedule for each country must be in accordance with the national or WHO recommendations.

Method of Administration:

Poliomyelitis Vaccine (Oral) Bivalent Type 1 and 3 must only be administered orally. Two drops are delivered directly into the mouth from the multi dose vial by dropper. For older children it may be preferred to avoid the possible bitter taste by first placing the drops on a sugar lump or in syrup. Care should be taken not to contaminate the dropper with saliva of the vaccine.

4.3 Contraindications
Poliomyelitis Vaccine (Oral) Bivalent Type 1 and 3 is contraindicated in individuals with known hypersensitivity to any component of the vaccine.

The vaccine is also contraindicated in those with primary immune deficiency disease or suppressed immune response from medication, leukaemia, lymphoma or generalized malignancy

4.4 Special Warnings and Precautions for Use
Poliomyelitis Vaccine (Oral) Bivalent Type 1 and 3 should not be injected.

In individuals already infected with a wild Type 1 or Type 3 Poliomyelitis virus, Poliomyelitis Vaccine (Oral) Bivalent Type 1 and 3 may not prevent or modify the course of the infection or disease.

The administration of Poliomyelitis Vaccine (Oral) Bivalent Type 1 and 3 should be postponed in individuals suffering from acute severe febrile illness, or persistent diarrhoea or vomiting. However, the presence of a minor infection, such as a cold, should not result in the deferral of vaccination. No adverse effects are produced by giving Poliomyelitis Vaccine (Oral) Bivalent Type 1 and 3 to a sick child.

Since diarrhea, vomiting and gastrointestinal infections may interfere with the administration of Poliomyelitis Vaccine (Oral) Bivalent Type 1 and 3, the dose received will not be counted as part of the immunisation schedule and should be repeated after recovery.

The attenuated poliomyelitis viruses multiply in the gut and may get excreted in faeces and may also be transmitted to the close contacts of the vaccinees; therefore, contacts of vaccinees should be warned for strict personal hygiene.

Non-immune persons in close contact with a recently vaccinated individuals may very rarely be at risk of vaccine-associated paralytic poliomyelitis (VAPP).

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

OPV is considered safe to administer to asymptomatic HIV-infected individuals. Previous vaccination with inactivated polio vaccine (IPV) is not a contraindication for the use of Poliomyelitis Vaccine (Oral) Bivalent Type 1 and 3.

4.5 Interaction with Other Medicinal Products and Other Forms of Interaction
Poliomyelitis Vaccine (Oral) Bivalent Type 1 and 3 can be given safely at the same time as IPV, measles, rubella, mumps, diphtheria, tetanus, and pertussis (DTP), DT, TT, Td (reduced diphtheria), BCG, hepatitis B, *Haemophilus influenzae* type b, pneumococcal, rotavirus vaccines, Yellow fever vaccine according to the vaccination schedule.

If Poliomyelitis Vaccine (Oral) Bivalent Type 1 and 3 cannot be given at the same time as other live attenuated vaccines, an interval of at least one month should be kept between such vaccinations.

Immunosuppressive therapies including irradiation, antimetabolites, alkylating agents, cytotoxic drugs and corticosteroids (used in greater than minimal doses), may reduce the immune response to vaccine.

4.6 Pregnancy and Lactation
Although there is no evidence that live attenuated polioviruses have an adverse effect on the foetus, in accordance with general principles, the vaccine should not be given to pregnant women unless they are exposed to a definite risk of infection with wild polioviruses. The risk benefit of the use of the vaccine should be evaluated in comparison to the use of inactivated polio vaccines.

Women of child-bearing age without immunity to polio should use contraception during 3 months following vaccination.

The administration of Poliomyelitis Vaccine (Oral) Bivalent Type 1 and 3 in lactating mothers has not been evaluated.

4.7 Effects on Ability to Drive and Use Machines
Effect of OPV on the ability to drive and operate machines is not known.

4.8 Undesirable Effects
In the Phase 3 trial, no related adverse event was reported.

Very rarely, vaccine associated paralysis poliomyelitis (less than one case per one million doses administered) has been reported with trivalent and bivalent OPV vaccines.

4.9 Overdose
No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Mechanism of Action
OPV mimics the immune response following infection with wild polioviruses, but without causing disease. Poliomyelitis Vaccine (Oral) Bivalent Type 1 and 3 OPV produces neutralizing antibodies against Type 1 and 3 Polioviruses and in the event of subsequent infection, this the neutralizing antibodies prevent the infection and protects the individual against poliomyelitis by preventing the spread of poliovirus to the nervous system. Apart from this, OPV induces mucosal immunity by replication in the intestinal mucosa and lymphoid cells, and in lymph nodes that drain intestine. The mucosal immunity induced by OPV is high, and it may play an important role in herd immunity by further reducing the amount of circulating wild type poliovirus.

5.2 Pharmacodynamic Properties
Pharmacotherapeutic group: Viral Vaccines

Poliomyelitis oral, bivalent, live attenuated. ATC code J07BF04

Immunological Data:

A phase III, observer-blind, randomized, controlled, study was conducted in 1080 infants aged 6-8 weeks of which 800 received Poliomyelitis Vaccine (Oral) Bivalent Type 1 and 3. Participants received three doses at 6, 10 and 14 weeks of age with minimum interval of 4 weeks between each dose. At 28 days after the third dose, seroconversion was >98%, while the seroprotection (poliovirus neutralizing antibody titre of ≥1:8) was >99%, against both type 1 and 3 polioviruses. Geometric mean titers (GMTs) were comparable between the Poliomyelitis Vaccine (Oral) Bivalent Type 1 and 3 and WHO prequalified SII bOPV (Bulk source - PT Biofarma; control group).

The Poliomyelitis Vaccine (Oral) Bivalent Type 1 and 3 demonstrated non-inferiority in terms of seroconversion against SII bOPV. The Geometric Mean Titres (GMTs) among three consecutively manufactured lots of Poliomyelitis Vaccine (Oral) Bivalent Type 1 and 3 were equivalent, thus demonstrating the clinical lot-to-lot consistency.

5.3 Pharmacokinetic Properties
Evaluation of pharmacokinetic properties is not required for vaccines.

6 NONCLINICAL PROPERTIES

6.1 Animal Toxicology or Pharmacology
A repeated-dose toxicity study of trivalent OPV (tOPV) in non-rodents [New Zealand White rabbits] showed that the vaccine is well tolerated. There were no toxicological alterations in the body weight, organ weights, clinical chemistry and pathologic parameters in the animals administered the vaccine. This trivalent OPV (tOPV) contains the same type 1 and type 3 polioviruses present in the BBio bivalent OPV (bOPV).

7. DESCRIPTION
Poliomyelitis Vaccine (Oral) Bivalent Type 1 and 3 is a light yellow to dark pink clear liquid in glass vial for oral administration.

8. PHARMACEUTICAL PARTICULARS

8.1 List of Excipients

Name of the Excipients	Quantity per 0.1 ml [Each dose of 2 drops]
Magnesium Chloride ($MgCl_2$)	1M
Polysorbate 80	12 µg
Water for Injections	q.s

8.2 Incompatibilities
The vaccine is not to be mixed with other vaccines/medicinal products.

8.3 Shelf-life
The product is stable for two years when stored at a temperature below -20°C.

8.4 Packaging Information
The vaccine is filled into USP Type-I glass vial, closed using Bromobutyl rubber stoppers and aluminium seals. The vaccine is available in 10 dose vial of 1 ml and 20 dose vials of 2 ml.

The 10 dose and 20 dose vials are packed into a box of 50 vials. Dropper is supplied with the vaccine vial.

8.5 Storage and Handling Instructions

Store in a freezer (at or below -20°C). The Vaccine is potent if stored at not higher than -20°C until the expiry date indicated on the vial.

In order to preserve optimal potency of the vaccine, exposure of the vaccine to ambient (non-refrigerated) temperatures should be kept to a minimum and exposure to sunlight should be avoided.

Transportation should be done under refrigerated conditions, particularly in hot climates.

When transportation or administration is not imminent, it is advisable to store the vaccine, if possible, at temperatures of -20°C or lower since this halts deterioration in vaccine potency.

It is recommended to store the vaccine in the original package in order to protect from light.

8.6 Special Precautions for Disposal

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

9 PATIENT COUNSELING INFORMATION

Prior to administration of Poliomyelitis Vaccine (Oral) Bivalent Type 1 and 3, inform the patient of the following:

- It is important to complete the immunization series as per national and or WHO recommendations.
- In the vast majority of cases there are no side effects. Very rarely, there may be vaccine associated paralysis (less than one case per one million doses administered).
- Report any adverse events to healthcare provider.

10. MARKETING AUTHORISATION HOLDER

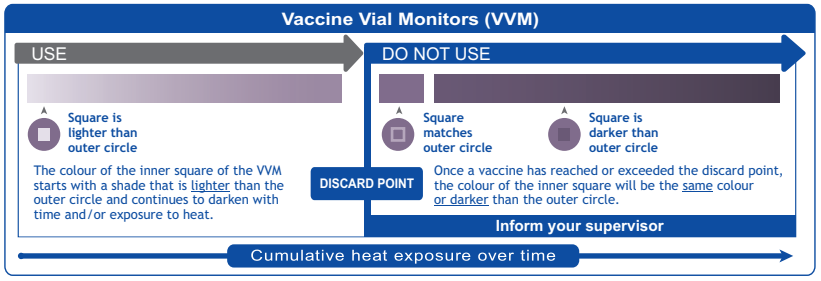
Serum Institute of India Pvt. Ltd.,
212/2, Hadapsar, Off Soli Poonawalla Road,
Pune - 411 028, Maharashtra, INDIA.

11. MARKETING AUTHORISATION NUMBER(S)

Manufacturing License No - 10 in Form 28-D.
Date of First Authorization: XX.XX.XXXX

12. DATE OF REVISION: Jan 2024

THE VACCINE VIAL MONITOR (VVM) (Optional)



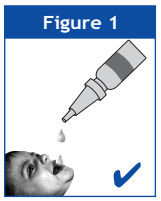
Vaccine Vial Monitors (VVMs) are part of the label on Poliomyelitis Vaccine (Oral) Bivalent Type 1 and 3 supplied through Serum Institute of India Pvt. Ltd. The colour dot which appears on the label of the vial is a VVM. This is a time-temperature sensitive dot that provides an indication of the cumulative 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. 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 outer circle, then the vaccine can be used. As soon as the colour of the central square is the same colour as the outer circle or of a darker colour than the outer circle, then the vial should be discarded.

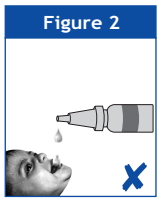
INSTRUCTIONS FOR USE:

The vial must first be shaken gently to avoid foaming, but sufficiently to obtain a homogenous mixture of the contents. Remove the flip top tear down seal, the rubber cap and fix the pre-sterilized plastic dropper supplied along with the vial. Remove the flip top from the aluminium part of seal along the direction of the indication on the flip. Pull the seal from the stoppered vial. Hold the vial inverted in tilted position and gently squeeze the plastic dropper to expel the vaccine drop-by-drop.

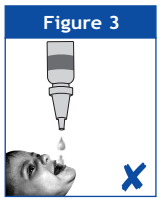
Directions for use of dropper during vaccine delivery



Hold the vial in tilted position during vaccine delivery into the mouth



Do not hold the vial horizontally for vaccine delivery into the mouth

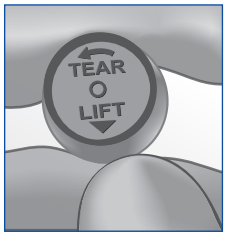


Do not hold the vial vertically for vaccine delivery into the mouth

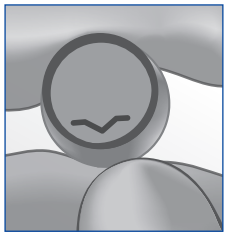
Directions for the dropper

1. Use specific droppers supplied by Serum Institute of India Pvt. Ltd.
2. Dropper should be discarded with the vaccine vial as re-use of droppers from one vial to another may lead to crack and leakage.
3. Always hold the vial in tilted position (ref. figure 1) for vaccine delivery.
4. Press the dropper gently just above the delivery nozzle with soft part of the fingers avoiding nail contact.
5. Bring vial along with dropper to upright position after delivery of each dose.
6. Put the nozzle cover back on the dropper when there is some time elapsed between two consecutive vaccine deliveries.

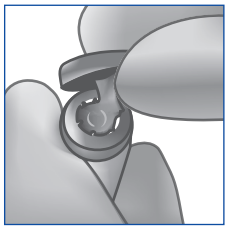
Directions for fixing the dropper on the OPV vial



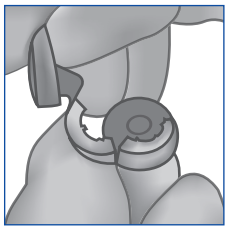
Or



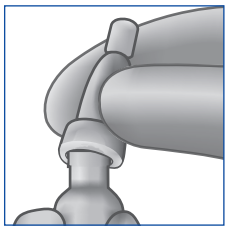
1. Remove the flip top of the cap by applying upward pressure at the point marked 'LIFT' or arrow
   Caution: Upward pressure has to be applied only at the marked point.



2. Once the flip top is detached, pull it over the edge of the seal and downward to the lower end of the vial mouth and rotate it counter clockwise in the direction of the arrow above the word 'TEAR'.
   Similar procedure to be used for arrow marked seal.



3. Remove the crimp cap completely. Rotating in the wrong direction will result in the flip top snapping off without removal of crimp cap



4. Remove the rubber stopper. Attach the dropper to the vial mouth.

Manufactured by:
SERUM INSTITUTE OF INDIA PVT. LTD.
212/2, Hadapsar, Pune 411 028, INDIA
Protection from birth onwards
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