Packaging Insert of Bivalent Poliomyelitis Vaccine Type 1 & Type 3, Live (Oral)

Bulk source: PT. Biofarma, Indonesia.

Note : The pictures of VVM & Diagrams for vaccine delivery shall also be printed in the colour as of text.

Size : 95x245mm (Front)

Bivalent Poliomyelitis Vaccine Type 1 & Type 3, Live (Oral)

DESCRIPTION
The Bivalent Poliomyelitis Vaccine Type 1 & Type 3, Live (Oral) (bOPV) contains suspensions of live attenuated Poliomyelitis type 1 & type 3 viruses (Sabin strains) propagated in Monkey kidney cells. Bivalent Poliomyelitis Vaccine Type 1 & Type 3, Live (Oral) complies with WHO recommendations.

COMPOSITION
Each dose of 2 drops (0.1 ml) contains
Polio virus (Sabin), grown on Monkey kidney cells
Type 1 Not Less Than $10^{6.0}$ $CCID_{50}$
Type 3 Not Less Than $10^{5.8}$ $CCID_{50}$
Kanamycin Acid Sulphate not more than 20 µg
Neomycin Sulphate not more than 20 µg
Stabilizer: 1 M $MgCl_2$
Phenol Red: Traces amount

PHARMACEUTICAL FORM
Oral suspension
The vaccine is presented as clear liquid, light reddish colored suspension for oral administration.

THERAPEUTIC INDICATION
Bivalent Poliomyelitis Vaccine Type 1 & Type 3, Live (Oral) is indicated for active immunization against infections caused by Type 1 and 3 Poliomyelitis viruses.

IMMUNIZATION SCHEDULE
Bivalent Poliomyelitis Vaccine Type 1 & Type 3, Live (Oral) is indicated for routine immunization against Poliomyelitis at birth and at 6, 10, 14 weeks or 2, 3, and 4 months and supplementary immunization activities (SIAs) in all age groups. The advised vaccination schedule for each country must be in accordance with the national or WHO recommendations.
In addition to bOPV routine immunization, one dose of IPV at 14 week is recommended to provide protection against Polio virus type 2 as risk mitigation.
Bivalent Poliomyelitis Vaccine Type 1 & Type 3, Live (Oral) can be administered at the same time with Measles, Mumps, Rubella, DTP, DT, TT, Td, BCG, Hepatitis B, *Haemophilus influenzae* type b and yellow fever vaccines and vitamin supplementation.

CONTRAINDICATIONS
Bivalent Poliomyelitis Vaccine Type 1 & Type 3, Live (Oral) is contraindicated in subjects with known hypersensitivity to neomycin or kanamycin, or to any other component of the vaccine.
In case of diarrhoea or vomiting (including gastrointestinal infection), the dose received will not be counted as part of the immunization schedule and it should be repeated after recovery.
In the vast majority of cases there are no side effects reported with Bivalent Poliomyelitis Vaccine Type 1 & Type 3(Oral). Very rarely, there may be vaccine-associated paralysis. Persons in close contact with a recently vaccinated child may very rarely be at risk of vaccine associated paralytic Poliomyelitis.
In case you experience any undesirable effect following administration of vaccine, please feel free to contact us at any of the following contact details: e-mail id: pvg@panaceabiotec.com; Fax no. : +91-11-41679069; Mob No: +91-9650138282

Immune Deficiency
Bivalent Poliomyelitis Vaccine Type 1 & Type 3, Live (Oral) is contraindicated in subjects suffering from primary and secondary immunodeficiency's including suppressed immune response from medication, leukaemia, lymphoma or generalized malignancy. For those persons it is recommended to use an inactivated Polio vaccine (IPV). However, according to the WHO Expanded Programme on Immunization (EPI) recommendations symptomatic and asymptomatic infection with human immunodeficiency virus is not a contraindication for immunization with Bivalent Poliomyelitis Vaccine Type 1 & Type 3, Live (Oral).

PRECAUTIONS
Bivalent Poliomyelitis Vaccine Type 1 & Type 3, Live (Oral) should under no circumstances be injected. It may not prevent or modify the course of the disease in subjects already infected with a wild Type 1 or Type 3 Poliomyelitis virus. The administration of Bivalent Poliomyelitis Vaccine Type 1 & Type 3, Live (Oral) should be postponed in subjects 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. The attenuated poliomyelitis viruses multiply in the gut. The faecal excretion of the vaccine viruses may persist for several weeks and may also be transmitted to the contacts of the vaccinees; contacts of vaccinees should therefore be warned about the need for strict personal hygiene.
Non-immune persons in close contact with a recently vaccinated subject may very rarely be at risk of vaccine-associated paralytic poliomyelitis.
Whenever Bivalent Poliomyelitis Vaccine Type 1 & Type 3, Live (Oral) is administered to an individual, it is good clinical practice to offer immunization to susceptible close contacts (such as unvaccinated parents) at the same time.
As with any vaccine, a protective immune response may not be elicited in all vaccinees. Previous vaccination with IPV is not a contraindication for the use of Bivalent Poliomyelitis Vaccine Type 1 & Type 3, Live (Oral).
Immunosuppressive treatment may reduce the immune response, may favour the multiplication of the vaccine viruses and may increase the length of excretion of the vaccine viruses in the stool. The effect on immunocompromised patients of the administration of Bivalent Poliomyelitis Vaccine Type 1 & Type 3, Live (Oral) has not been evaluated in clinical studies.

Pregnancy
Although there is no evidence that live attenuated polioviruses have adverse effects 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.

Lactation
The effect on breast-fed infants of the administration of Bivalent Poliomyelitis Vaccine Type 1 & Type 3, Live (Oral) to their mothers has not been evaluated in clinical studies. No known contra-indication has been established. The vaccine may be administered to a lactating mother.

Women of childbearing potential/ contraception
Non immune woman of child-bearing age should use contraception during 3 months following vaccination.

Effects on ability to drive and use machines
There have been no studies to investigate the effect of Bivalent Poliomyelitis Vaccine Type 1 & Type 3, Live (Oral) on driving performance or the ability to operate machinery. Nevertheless, considering the adverse event profile of Bivalent Poliomyelitis Vaccine Type 1 & Type 3, Live (Oral) it is unlikely that the vaccine has an effect on the ability to drive and use machines.

Overdose
No reports of overdose with Panacea Biotec's Bivalent Poliomyelitis Vaccine Type 1 & Type 3, Live (Oral) have been received.

Incompatibilities
This biological product must not be mixed with other biological products.

ADVERSE REACTIONS
In the vast majority of cases there are no side effects. Very rarely, there may be vaccine associated paralysis (one case per one million doses administered). Persons in close contact with a recently vaccinated child may very rarely be at risk of vaccine associated paralytic Poliomyelitis.

ADMINISTRATION
Vaccines should be inspected visually for any particulate matter prior to administration.
Bivalent Poliomyelitis Vaccine Type 1 & Type 3, Live (Oral) must be administered orally. Two drops are delivered directly into the mouth of vaccinee from the multidose 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 a multidose dropper with saliva of the vaccinee. Once opened, multi-dose vials should be kept between +2°C and +8°C.
Multi-dose vials of Bivalent Poliomyelitis Vaccine Type 1 & Type 3, Live (Oral) from which one or more doses of vaccine have been withdrawn during an immunization session may be used in subsequent immunization sessions for up to a maximum period of 4 weeks, provided that all of the following conditions are met (as described in the WHO policy statement: The use of opened multi dose vials in subsequent immunization sessions. WHO/V&B/00.09):

- The expiry date has not passed;
- The vaccines are stored under appropriate cold chain conditions;
- The vaccine vial septum has not been submerged in water;
- Aseptic technique has been used to withdraw all doses;
- The vaccine vial monitor (VVM), if attached, has not reached the discard point (see figure).

After opening, immediate use is recommended.
When distribution 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. If the vaccine has been accidentally exposed to high environmental temperatures, it is recommended that the vaccine be used immediately or stored ideally at –20°C or at 2-8°C until administration under condition that the VVM allows its use.

PHARMACOLOGICAL PROPERTIES
Pharmacokinetic properties
Evaluation of pharmacokinetics is not required for vaccines.

Size : 95x245mm (Back)

Pharmacodynamics properties
On the basis of clinical study and published literature, it can be estimated that the seroresponse against Types 1 and 3 Poliomyelitis viruses will be at least equal to those obtained with a trivalent oral Poliomyelitis vaccine (tOPV).

Preclinical safety data
As the safety of OPV variants has been proven through its extensive usage over the years, no separate pre-clinical study was performed for bOPV (BS:PT. BioFarma].

Clinical Studies:
There were 3 clinical studies conducted on bOPV (Bulk PT Biofarma)
1. A Phase IV study Protocol No. PBL/CR/0042008/CT :
.A randomized, controlled, 5-arm, comparative study was conducted in 900 newborn to evaluate the immunogenicity and reactogenicity of Trivalent Oral Polio Vaccine (tOPV) versus Monovalent Type 2 Oral Polio Vaccine (mOPV2) & Monovalent Type 3 Oral Polio Vaccine (mOPV3); and Bivalent Oral Polio Vaccine (bOPV) versus Monovalent Type 1 Oral Polio Vaccine (mOPV1) & Monovalent Type 3 Oral Polio Vaccine (mOPV3). In this study, the seroconversion rate for Type 1 Polio virus and Type 3 Polio virus with bOPV was 80.3% and 70.9% respectively. These results were comparable to the seroconversion achieved with mOPV1 vaccine for Polio virus Type 1 and with mOPV 3 vaccine for Type 3 Polio virus. There were total 19 SAE's occurred in the study. Among the 19 SAE's, there was one SAE in bOPV arm. No SAE were related to study vaccine.
2. A Phase III study Protocol No. PBL/CR/2010/02/CT:
A comparative Phase III Clinical Trial of bOPV (Bulk Sanofi) was conducted in 265 infants using bOPV (PT Biofarma) as comparator to evaluate immunogenicity & reactogenicity The results of immunogenicity and reactogenicity of bOPV manufactured from two bulk sources i.e. Sanofi Pasteur France and PT. BioFarma, Indonesia were found to be comparable after administration of single dose to healthy infants of 6 to 10 weeks. The single dose seroconversion rate for Type 1 Polio virus was 82.4% and 82.9% for bOPV (Sanofi) and bOPV (PT. BioFarma) respectively and the seroconversion for Type 3 Polio virus was 80.8% and 77.5%. for bOPV (Sanofi) and bOPV (PT. BioFarma) respectively. There was one SAE sepsis with acute gastroenteritis with diselectrolytemia with paralylic lleus in the study and was not causally linked to the study vaccine. There were no AEs reported related to bOPV.
3. A Phase IV Study Protocol No. PBL/CR/2011/02/CT:
Another clinical study was performed to assess the mucosal immunity to Polioviruses after a supplemental dose of bOPV or IPV in 990 children in northern India. Seroconversions induced to Poliovirus type 1 at day 28 after the administration of a bOPV dose were 14.3%, 12.9%, and 42.4% for subjects in 6 to 11 month, 5-years, and 10 years age groups respectively. Seroconversions induced to Poliovirus type 3 at day 28 after the administration of a bOPV dose were 14.1 %, 15.9%, and 53.5% for subjects in 6 to 11 month, 5-years, and 10 years age groups respectively. There were no AEs related to study vaccine.
Immunogenicity results of clinical studies do not demonstrate interference by co-administered EPI vaccines.

Periodic Safety Updated Report (PSUR Data):
During the reporting period from 2009 to till updation of current package insert, there were total 24 unlisted Adverse Reaction (07 Gastroenteritis, 01 Anemia, 01 Anal abscess, 01 Sepsis neonatal , 01 Abdominal distension, 02 Diarrhea, , 01 Ileus paralytic, 01 Vomiting, 01 Pyrexia, 01 Blood electrolyte abnormal, 02 Dehydration, 01 Malnutrition, 01 Asthma, 01 Pneumonitis, 02 Wheezing reported and out of these 10 were reported from clinical studies which were unrelated to bOPV. 2 serious listed ADR of VAPP (Vaccine associated Paralytic Polio) reported from literature which was related to bOPV.

Geographical exposure:
In addition to India, bOPV was extensively used in the countries of Asian and African region .

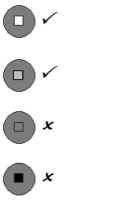
SHELF LIFE
Assigned shelf life is 24 months when stored at minus 20°C.

STORAGE
Vaccine is potent if stored at not higher than minus 20° C until the expiry date indicated on the vial. It can be stored for upto six months between +2° C and +8° C.

PRESENTATION
The vaccine comes in vials of 20 doses.
Vaccine Vial Monitors (VVMs) are part of the label on all Bivalent Poliomyelitis Vaccine Type 1 & Type 3, Live (Oral) vaccine vials. These VVMs are supplied by TEMPTIME Corporation, U.S.A. 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 on exposure to high temperature. As long as the colour of this square is lighter than the colour of the outer circle 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, the vaccine vial should be discarded.

Figure of the Vaccine Vial Monitor (VVM)

The vaccine vial monitor ...



Inner square is lighter than outer circle.
If the expiry date has not been passed, USE the vaccine.

At a later time, inner square still lighter than outer circle.
If the expiry date has not been passed, USE the vaccine.

Discard point :
Inner square matches colour of outer circle.
Do not use the vaccine.

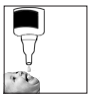
Beyond the discard point :
Inner square darker than outer circle.
Do not use the vaccine.

Directions for use of droppers
1. Use specific droppers supplied by Panacea Biotec Ltd.
2. Dropper should be discarded with 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. Fig. as below) 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 back 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.

Holding Position of Dropper During Vaccine Delivery

Fig. 1  ✔ **Hold the vial at tilted position** during vaccine delivery into the mouth

Fig. 2  ✘ **Do not hold the vial horizontally** for vaccine delivery into the mouth

Fig. 3  ✘ **Do not hold the vial vertically** for vaccine delivery into the mouth

Panacea Biotec
Innovation in support of life

Bulk source: PT. Biofarma, Indonesia.

Manufactured by:
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