طبقا لقرار اللجنة العلمية المتخصصة للمستحضرات الحيوية
بجلستها في ٢٠٢٠/٧/١٦ .

Summary of Product Characteristics

1. Name of the Medicinal Product

   Poliomyelitis (Live) Vaccine Type I Type III (Human Diploid Cell), Oral

   1.1 Strength

   2.0mL/20 doses/vial

   1.2 Pharmaceutical form

   Oral liquid

2. Qualitative and Quantitative Composition

   2.1 Qualitative declaration

   Poliomyelitis (Live) Vaccine Type I Type III (Human Diploid Cell), Oral (bOPV) is a vaccine containing suspensions of types I and III live attenuated polioviruses (Sabin strain). The product, which is prepared by inoculation of the type I and III attenuated polio virus strains into the human diploid cells and then the virus was incubated and harvested, is a reddish orange liquid. One Molar magnesium chloride ($MgCl_2$) is added as a stabilizer. The production process of bOPV complies with WHO's requirements.

   2.2 Quantitative declaration

   Each dose of 2 drops (0.1mL) contains

   Polio virus (Sabin)

   OPV Sabin Bivalent strain type I and III viruses: Not less than 6.21Lg$CCID_{50}$ (or $10^{6.21}$ $CCID_{50}$) /dose

   OPV Sabin strain type I viruses: Not less than 6.0 Lg$CCID_{50}$ (or $10^{6.0}$ $CCID_{50}$) /dose

   OPV Sabin strain type III viruses: Not less than 5.8 Lg$CCID_{50}$ (or $10^{5.8}CCID_{50}$) /dose

   Stabilizer: 1 M $MgCl_2$

   Residual Antibiotics: Gentamicin not more than 50 ng/dose

3. Pharmaceutical Form

2.0mL/20 dose/vial, Oral Liquid

The product is a reddish orange, clear liquid without visible particle.

4. Clinical Particulars

4.1 Therapeutic indication

Poliomyelitis (Live) Vaccine Type I Type III (Human Diploid Cell), Oral indicated for active immunization against type I and III polioviruses.

4.2 Posology and method of administration

bOPV must only be administered orally. Two drops are delivered directly into the mouth from the multi-dose vial by dropper supplied with the vaccine. Care should be taken not to contaminate a multi-dose dropper with saliva.

The vaccines should be naturally thawed into liquid at room temperature for 10 minutes before use. Thawing with heat is strictly prohibited.

Once opened, multi-dose vials should be kept between +2℃ and +8℃.

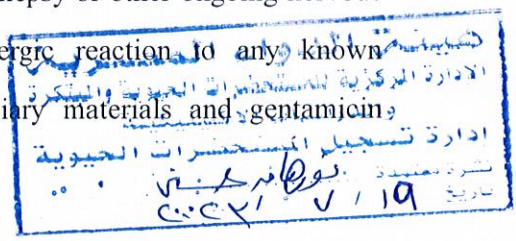
Multi-dose vials of bOPV from which one or more doses of vaccine have been removed during an immunization session may be used in subsequent immunization sessions for up to a maximum of 4 weeks, provided that all of the following conditions are met (as described in the WHO Policy Statement: Multi-dose Vial Policy (MDVP) Revision 2014 WHO/IVB/14.07).

- The vaccine is currently prequalified by WHO.
- The vaccine is approved for use for up to 28 days after opening the vial, as determined by WHO.
- The expiry date of the vaccine has not passed.
- The vaccine vial has been, and will continue to be, stored at WHO- or manufacturer- recommended temperatures; furthermore, the vaccine vial

monitor, if one is attached, is visible on the vaccine label and is not past its discard point, and the vaccine has not been damaged by freezing.

4.3 Contraindication

For those suffering from acute diseases, serious chronic diseases, acute attack of the chronic diseases, fever, uncontrolled epilepsy or other ongoing nervous system diseases or with a history of allergic reaction to any known components in the vaccine, including auxiliary materials and gentamicin sulphate, the vaccine is contraindicated.



4.4 Special Warning and Precaution for use

In case of diarrhoea and/or vomiting (as well as gastro-intestinal infection), the dose received will not be counted as part of the immunization schedule and should be repeated after recovery.

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.

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 stools.

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

4.5 Interaction with other medicinal products and other forms of interaction

bOPV can be given safely and effectively at the same time as the vaccines recommended by Expanded Programme on Immunization (EPI) if this fits into the vaccination schedule.

If bOPV cannot be given at the same time as live attenuated vaccines, an interval of at least one month should be left between both vaccinations.

4.6 Fertility, 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.

4.7 Effect on ability to drive and machine

N/A

4.8 Undesirable effects

Very common (may affect more than one in 10 people) adverse reactions: mild fever, diarrhea. Common adverse reactions (may affect less than one in 10 people but more than one in 100 people): irritability and vomiting. (The result above is based on a clinical trial in China)

Generally, these will not require special treatment, but can be treated according to specific symptoms when needed.

Very rarely, there may be vaccine-associated paralysis (one case per 1 million doses administered). Persons in close contact with the vaccinees may very rarely be at risk of vaccine associated paralytic poliomyelitis.

4.9 Overdose

N/A

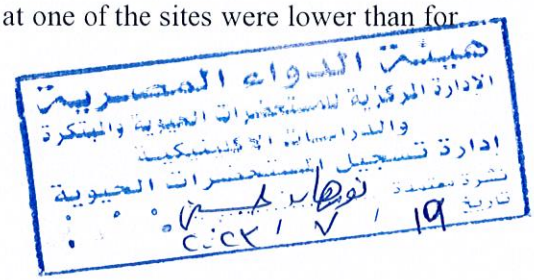
5. Pharmacological properties

5.1 Pharmacodynamics properties

In the clinical study in China, Serum conversion rate and 4-fold growth rate: The type I & III serum conversion rate (4-folds growth rate) of the trial vaccine groups (the 2wIPV+bOPV group and the wIPV+2bOPV group) showed no significant difference from that of the control vaccine group (2wIPV+tOPV/wIPV+2tOPV) and those of other groups, and the type I & III serum conversion rate (4-fold growth rate) of the bOPV sequential group was not inferior to that of the tOPV sequential group; The type II serum conversion rate (4-folds increase rate) of the group 2wIPV+bOPV also showed no significant difference from that of the tOPV sequential group and those of other control groups like IPV/OPV, and only the type II serum conversion rate (4-fold growth rate) of the wIPV+2bOPV group was lower than those of the other groups, with significant difference. Antibody level: The type I antibody GMT of the trial vaccine group (2wIPV+bOPV/wIPV+2bOPV) showed no significant difference from that of the control vaccine group (2wIPV+tOPV/wIPV+2tOPV) and the tOPV control group, which, however, was higher than that of the wIPV group; The type III antibody GMT of the group 2wIPV+bOPV was higher than that of the group wIPV+2bOPV, and also significantly higher than that of the sequential group tOPV as well as the control groups wIPV and tOPV; The type II antibody GMT of the 2wIPV+bOPV was higher than that of the group wIPV+2bOPV, and the type II antibody GMT of the sequential group bOPV was significantly lower than that of the sequential group tOPV and those of the control groups wIPV and tOPV.

In the clinical study in Kenyan BIBP two batches of products have good consistency between batches. The criterion for non-inferiorty to the comparator vaccine was that the lower limit of the 2-sdied 95% CI for the difference in proportions between the BIBP bOPV and the comparator vaccine be greater than -10 percentage points. The difference (and 95% CI) for type 1 was 1.5 (-0.5 to 4.6) and for type 3 was 2.2 (-0.1 to 5.6). Seroconversion rates

in the BIBP arms were high (greater than 98% for both serotypes in both lots) and never less than that of the control arm. Further, post-vaccination seroprotection rates were also very high (99.1% for both serotypes). The prespecified criteria for non-interference for hepatitis B vaccine were met. For HBV, the results were consistent across the arms of the study at both sites. Seroprotection rates for the BIBP and control arms were not significantly different: 93.7% and 93.8%, respectively. The difference in percentage points (and 95% CI) was -0.09 (-3.86 to 4.48). Similarly, the GMTs were similar, with the ratio (and 95% CI) of the BIBP to control arms 1.20 (0.89 to 1.63). The prespecified criteria for non-interference were also met for rotavirus vaccine. The ratio (and 95% CI) of GMTs of the BIBP to control arms was 0.99 (0.71 to 1.38). The GMTs for lot 1 at one of the sites were lower than for lot 2, but the overall criteria were met.



5.2 Pharmacokinetics properties

N/A

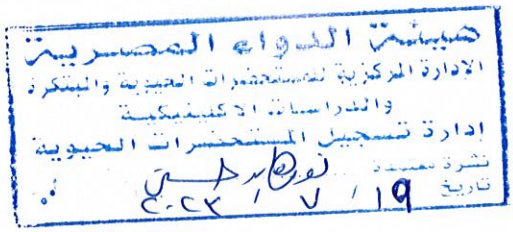
5.3 Preclinical safety data

108 monkeys with 36 controls are tested with each batch of vaccine bulk, bulk sample (reference) is injected into monkey lumbar cord at the first to second lumbar intervertebral space, 0.1 mL per monkey, 5.5 – 6.5 lgCCID$_{50}$/0.1 mL. Follow up for 17 – 18 days for detecting of any local allergic reactions such as papule or red and swollen, itching or decrustation, or any scratch, papule, blood scab, chromatosis, eczema or moss-like changes to the skin caused by scratching. Monkeys will be executed with euthanasia when completing the observation, and followed by gross anatomy, detect if there is effusion in abdominal cavity, or any adhesion or nodule to the abdomen organs, or swelling spleen, malposition of epiploic, effusion in thoracic cavity, or malposition, colour abnormal or size of heart, lungs, thymus gland and

mediastinum, or any effusion in cardiac chambers, adhesion between heart and pericardium.

During the testing, Monkeys were executed with euthanasia when completing the observation and there were no abdomen organs were detected following by anatomy.

Pathological examination is carried out for brain and spinal nerves system to detect any damage to neurons.



6. Pharmaceutical particulars

6.1 List of excipients

Stabilizer: $MgCl_2$

Earle's solution: NaCl, Glucose, $CaCl_2$, NaH_2PO_4, KCl, $MgCl_2$, Phenol red, NaOH, Lactoalbumin hydrolysate, L-Cysteine hydrochloride monohydrate.

6.2 Incompatibilities

bOPV is administered orally and there is no purification process in the bOPV manufacturing and also no QC impurity testing. A lot of process parameters have no impact on the product quality, only on its quantity. Therefore, the compatibility study is not conducted.

6.3 Shelf life

24 months

6.4 Special precaution for storage

Vaccine is potent if stored at minus 20°C or below until the expiry date indicated on the vaccine vial label.

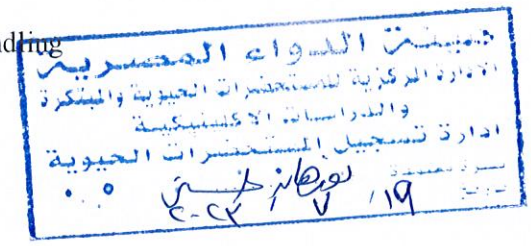
It can be stored for up to six months between +2°C and +8°C, or can be re-frozen at minus 20°C for up to six months.

6.5 Nature and content of container

The liquid bOPV vaccine is contained in 2.0 mL glass vials, stoppered with chlorinated butyl rubber stopper closures, type slotted and closed with aluminum foil caps.

6.6 Special precautions for disposal and other handling

Refer to the section 4.3 and 4.4



7. Marketing authorization holder

Beijing Institute of Biological Products Co., Ltd.

Address: Beijing Economic and Technological Development Area, Boxing 2 Road No.6, 9.

8. Marketing authorization number(s)

GYZZS20150015

9. Date of first authorization/renewal of the authorization

Date of first authorization: November 19th, 2015

Date of renewal of authorization: October 30th, 2020

10. Date of revision of the text

March 2022