Registration No. 2C 1/57(B)

Importer / Manufacturer: Bionovel Co., Ltd./Panacea Biotech Ltd.

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICAL PRODUCT
POLPROTEC®

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
One dose of 0.5 ml contains:

- Inactivated Salk Poliovirus type 1: 40 DU
- Inactivated Salk Poliovirus type 2: 8 DU
- Inactivated Salk Poliovirus type 3: 32 DU
- 2-phenoxyethanol: 2.5 mg
- Formaldehyde: 12.5 μg
- Sodium Phosphate buffer: 0.04 ml
- Dilution fluid: 0.04 ml
- Water for Injection: q.s.

3. PHARMACEUTICAL FORM
Suspension for injection.

POLPROTEC® [Inactivated Poliomyelitis Vaccine (IPV)] is a trivalent vaccine containing an aqueous suspension of Poliovirus Types 1, 2 and 3 (Salk strains) grown in Vero Cell Culture. The poliovirus obtained from the Vero Cell Culture are concentrated, purified by various physicochemical methods and inactivated by formaldehyde. The final vaccine also contains formaldehyde as a stabilizer and 2-phenoxyethanol as an antimicrobial preservative and phenol red as pH indicator. Antibiotics (neomycin, streptomycin and polymyxin B) and bovine serum albumin are used in production and likely present in trace amount.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications

POLPROTEC® is indicated for the prevention of poliomyelitis in infants, children and adults, for primary vaccination and as a booster.

Infants, children and adolescents
It is recommended that all infants, unimmunized children and adolescents not previously immunized should be immunized routinely against paralytic poliomyelitis.

Adults
It is necessary to review the immunization status of all adults at risk of exposure to poliovirus. A primary series of IPV is recommended for unvaccinated adults at increased risk of exposure to poliovirus.

The following categories of persons are at increased risk of exposure to poliovirus:
- Travelers to countries where polio is still transmitted or may be at risk;
- Laboratory workers who handle specimens that may contain polioviruses;
- Health care workers in close contact with people who can shed wild or vaccine strains of poliovirus;
- Unimmunized parents or child care workers who will be caring for children in countries where OPV is used;
- Members of communities or groups of individuals having the disease caused by wild poliovirus.

IPV can be used for completing immunization series in cases of previous clinical poliomyelitis (usually due to only a single poliovirus type) or incomplete immunization with OPV.
Immune deficiency and altered immune status

Patients with immuno-deficiencies status are at a greater risk of developing paralysis when exposed to poliovirus. Oral polio vaccine is contraindicated in such a patient. Individuals infected with immunodeficiency virus (HIV), both asymptomatic and symptomatic, altered immune status due to disease and compromised immune system due to treatment with corticosteroids should be immunized with IPV according to the dosage schedule given below. Patients with altered immune status may or may not develop a protective immune response after administration of IPV.

4.2 Posology and method of administration

Primary vaccination of children:
From 6 weeks of age, POLPROTEC® may be administered following the 6, 10, 14-week schedule, as per the recommendations of the Expanded Programme on Immunization of the World Health Organization.
From 2 months of age, 3 successive injections of 0.5 ml POLPROTEC® should be administered at intervals of one or two months.

Primary vaccination in adults:
For non vaccinated adults, two successive injections of 0.5 ml must be given at intervals of one month.

Booster:
For children: If the primary series begins earlier (for example, with a 6-week, 10-week and 14-week schedule) then a booster dose should be administered after an interval of ≥ 6 months (for a 4-dose schedule).
For adults: The 3rd dose of IPV (booster) is administered 8 to 12 months after the 2nd injection.
Persons fully immunized against poliomyelitis and leaving to areas having a high incidence of poliomyelitis are advised to re-vaccinate with a single-dose of polio vaccine approx. 1 month before departure, particularly when their last immunization was more than 15 years ago.

Preparation for Administration
Before injection, SHAKE THE PRE-FILLED SYRINGE.
Examine the vaccine for the presence of foreign particles. If particles are observed, do not administer the product.
Administer POLPROTEC® intramuscularly.
Do not inject intravenously.
Lateral aspect of the mid thigh is the preferred site in infants and small children. In older children and adults, it should be administered in deltoid area.
For patients with thrombocytopenia or bleeding disorders the injection should be given subcutaneously.

4.3 Contraindication
The vaccine should not be administered to subjects with known hypersensitivity to any component of the vaccine (including 2-phenoxyethanol, formaldehyde, neomycin, streptomycin, polymyxin B and bovine serum albumin), or to subjects that have shown any signs of hypersensitivity after previous administration of IPV vaccine. Vaccination of persons with an acute, febrile illness should be deferred until recovery.

4.4 Special warnings and precautions for use
Take special care with the vaccine if the child:
- Has thrombocytopenia or a bleeding disorder, because of the bleeding that can occur during intramuscular administration of the vaccine.
- Is taking a treatment that suppresses the immune response or has an immune deficiency disorder, in which case 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. Vaccination of
subjects with chronic immunodeficiency, such as HIV infection, is nevertheless recommended even if the immune response might be limited by the underlying illness.

- This vaccine may also be indicated for subjects for whom the oral vaccine is contraindicated and as a booster for subjects previously vaccinated with the oral vaccine.

As with any vaccine, immunization with IPV may not protect 100% of susceptible persons. Aseptic technique must be used for injection.

POLPROTEC® should not be administered into the buttocks due to possible nerve injury, nor by the intradermal route, since these methods of administration may induce a weaker immune response. Do not inject into a blood vessel.

POLPROTEC® should not be used for control of outbreaks of poliomyelitis if OPV is available.

Before administration, take all appropriate precautions to prevent adverse reactions. This includes a review of the patient’s history concerning possible hypersensitivity to the vaccine or similar vaccine, previous immunization history and the presence of any contraindications to immunization. As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic event following the administration of the vaccine.

Before administration of vaccine, health-care providers should inform the patient, parent or guardian of the benefits and risks of immunization, inquire about the recent health status of the patient and comply with any local requirements regarding information to be provided to the patient before immunization and the importance of completing the immunization series.

It is important that the patient, parent or guardian be questioned concerning any symptoms and/or signs of an adverse reaction after a previous dose of vaccine.

4.5 Interaction with other medical products and forms of interaction

Use with other vaccine

Concomitant administration, of other parenteral vaccines, with separate syringes at separate sites, is not contraindicated. There is no historical data demonstrating interference of antibody responses to Diphtheria, Tetanus, Pertussis (Whole Cell), Hepatitis B (rDNA) and Haemophilus Type b Conjugate Vaccine (Adsorbed) IP used concomitantly with IPV on the immunological endpoints accepted for clinical protection.

4.6 Pregnancy and lactation

This vaccine may be used during pregnancy, if required. Breast feeding is not a contraindication.

4.7 Effects on the ability to drive and use machines

It is assumed that poliomyelitis vaccine has no effect on driving skills or the capability to operate machines.

4.8 Undesirable effects

In the trial conducted to compare the immunogenicity and safety of POLPROTEC® with a WHO prequalified vaccine, 575 subjects received at least one dose of the vaccine (safety cohort). In this study post-vaccination adverse events (solicited and unsolicited) were recorded. Pain at the injection site was the most common local reaction reported by 31.94% subjects treated with POLPROTEC®. Other local reactions reported were erythema, swelling and induration which were reported by 14.58%, 1.39% and 1.04%, respectively. Axillary Temperature of ≥ 38°C (≥ 100.4°F) was reported in 56.6% of the subjects. Other solicited symptoms reported in the trial included loss of appetite/change in feeding habits, persistent crying, irritability/restlessness, sleepiness, diarrhea and vomiting. Because IPV was given in a different site but concomitantly with Diphtheria, Tetanus, Pertussis (Whole Cell), Hepatitis B (rDNA) and Haemophilus Type b Conjugate Vaccine (Adsorbed) IP (Easyfive®), these systemic reactions could not be attributed to a specific
vaccine. All solicited systemic symptoms were mild/moderate in intensity. The incidence of each systemic symptom over all doses was similar in the comparator group.

Other adverse events reported in the trial include:

General disorders and administration site conditions: Influenza like illness
Infections and infestations: Nasopharyngitis
Respiratory, thoracic and mediastinal disorders: Cough, Nasal congestion
Metabolism and nutrition disorders: Decreased appetite
Gastrointestinal disorders: Diarrhea

All the unsolicited AEs were mild/moderate in intensity.

Immune response to a supplemental dose of different poliovirus vaccines in a population with a history of multiple OPV doses was studied in a clinical trial. The study also assessed the adverse events reported in each trial participant for 28 days post vaccination. The number and severity of local adverse events after IPV administration was low. Only 3% had mild swelling or redness after intramuscular injections and only one case presented local inflammation associated with fever. There were no differences in local events among the study groups. These results confirm the low reactogenicity of IPV for intramuscular administration. On the other hand, there were a high number of infectious events during the 28 days study follow-up. These events consisted of diarrhea (±fever, vomiting or signs of upper respiratory infection), upper respiratory infection and other AEs reported in the trial subjects. Three SAEs were reported after intramuscular administration of POLPROTEC®. In all these cases symptoms consisted of diarrhea, vomiting and/or fever that required hospitalization for rehydration with intravenous fluids. It was concluded that there was no causal association between receiving the study vaccine and the adverse events.

The following adverse events, though not necessarily reported during clinical trials of POLPROTEC®, have been reported following administration of other IPV vaccines:

4.9 Overdose
N/A

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Inactivated Poliomyelitis Vaccine induces the production of neutralizing antibodies against each of the three types of viruses. Administration of the second dose results in rapid increase of antibody levels indicating existence of immunological memory. IPV is able to induce secretory antibody (IgA) produced in the pharynx and gut and reduces pharyngeal excretion of poliovirus. VAPP has not been reported in association with administration of IPV.
Panacea Biotec Limited has conducted an open labeled, randomized, multicentre, comparative study of its POLPROTEC® Vaccine. The objective of the study was to compare the immunogenicity and safety of POLPROTEC® with a WHO prequalified IPV Vaccine when administered as per primary vaccination schedule of EPI. A total of 624 subjects were enrolled for the study and were randomized in a 1:1 ratio to receive 3 doses of either POLPROTEC® or the comparator vaccine at 6, 10 and 14 weeks of age. Of the 624 subjects enrolled in the study 565 completed the study as per the protocol and the titers from these were used for immunogenicity analysis. Analysis of post vaccination antibody titers showed that seroconversion rate against polio type 1, type 2 and type 3 was 92.88%, 94.31% and 98.58% in the subjects treated with POLPROTEC®. The adjusted GMT ratios obtained for Polprotec over comparator group were 0.92, 1.19 and 1.22 for Type 1, 2 and 3 serotypes, respectively. The seroprotection/immune response rates and the antibody GMTs for concomitantly administered DTwP-HepB-Hib (Easyfive®) vaccine were found to be similar in the two treatment groups. Three batches of POLPROTEC® were used in the test arm of the trial. The POLPROTEC® vaccine showed a good lot-to-lot consistency with respect to GMT with respect to the three vaccine lots used in the trial. In this clinical study, POLPROTEC® was found to be non inferior to the WHO prequalified comparator IPV Vaccine.

A study was conducted to compare the immune response to a supplemental dose of different poliovirus vaccines in a population with a history of multiple OPV doses. The study vaccines included POLPROTEC® and IPV by another manufacturer. Healthy infants 6-9 months were enrolled and randomized to receive one of the study vaccines. Antibody titers were measured in serum by neutralization assays at baseline (before first vaccination) and at 7 and 28 days post vaccination. Seroprevalence (seropositive children) was defined as reciprocal titers ≥8 and seroconversion as being seronegative at baseline and seropositive at 28 days. Booster was defined as an increase in antibody titers by ≥4-fold for those individuals with baseline reciprocal antibody titers ranging between 8-362. Seroconversion rates after intramuscular administration of POLPROTEC® were 100% for type 1 and 2 and 91% for type 3. Boosting by ≥4-fold in antibody titers for children seropositive at baseline occurred in 85% for type 1 and 3 and 72%, for type 2. As a result median titers 1 month after vaccination were very high for all three types in the population, ≥ 1448 for type 1 and 2, and 362 for type 3. There were no differences in performance between POLPROTEC® and comparator vaccine.

5.2 Pharmacokinetic properties
N/A

5.3 Preclinical safety data
N/A

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
2-phenoxyethanol, Formaldehyde, Sodium Phosphate buffer, Dilution fluid, Water for Injection

6.2 Incompatibilities
N/A

6.3 Shelf life
36 months from the date of manufacturing when stored at +2°C to +8°C.

6.4 Special precautions for storage
The vaccine should be stored and transported at temperature at +2°C to +8°C until the expiry date indicated on the label.
DO NOT FREEZE.

6.5 Nature and contents of container
Single dose prefilled syringe containing 0.5 ml vaccine with LuerLok & PRTC (plastic rigid tip cap).

6.6 Special precautions for disposal and other handling
PREPARATION FOR INJECTION
Remove the prefilled syringe from the blister pack. Holding the syringe barrel, remove the PRTC from the tip of syringe. The PRTC design makes the tip cap easy to open and promote aseptic technique by reducing risk of syringe tip contamination during cap removal. Attach the needle to the LuerLok syringe. LuerLok Adaptor design helps in maintaining “Needle Integrity” by not allowing needle to touch any other material. In the unusual event of the piston rod becoming loose or falling off, screw it clockwise into the plunger in order to secure it.
Each prefilled syringe should be used only once.
The peel-off label on the barrel of the syringe is to be pasted on the vaccinee’s vaccination card for future reference.

7. MARKETING AUTHORISATION HOLDER
Bionovel Co., Ltd.
1993 Moo 4 Soi Sukhumvit 115 (Apichart)
Sukhumvit Road Theparak Muang Samutprakarn 10270
Tel. +662 384 7472 Fax. +662 757 7551

8. MARKETING AUTHORISATION NUMBER(S)
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January 28, 2014

10. DATE OF REVISION OF THE TEXT
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