**DESCRIPTION**

IPOL®, Poliovirus Vaccine Inactivated, produced by Sanofi Pasteur SA, is a sterile suspension of three types of poliovirus: Type 1 (Mahoney), Type 2 (MEF-1), and Type 3 (Saukett). IPOL vaccine is a highly purified, inactivated poliovirus vaccine with enhanced potency. Each of the three strains of poliovirus is individually grown in vero cells, a continuous line of monkey kidney cells cultivated on microcarriers. (1) (2) The cells are grown in Eagle MEM modified medium, supplemented with newborn calf bovine serum tested for adventitious agents prior to use, originated from countries free of bovine spongiform encephalopathy. For viral growth, the culture medium is replaced by M-199, without calf bovine serum. This culture technique and improvements in purification, concentration, and standardization of poliovirus antigen produce a more potent and consistent immunogenic vaccine than the inactivated poliovirus vaccine (IPV) available in the US prior to 1988. (3) (4) After clarification and filtration, viral suspensions are concentrated by ultrafiltration, and purified by three liquid chromatography steps: one column of anion exchanger, one column of gel filtration, and again a column of anion exchanger. After re-equilibration of the purified viral suspension with Medium M-199 and adjustment of the antigen titer, the monovalent viral suspensions are inactivated at +37°C for at least 12 days with 1:4,000 formalin.

Each dose (0.5 mL) of trivalent vaccine is formulated to contain 40 D antigen units of Type 1, 8 D antigen units of Type 2, and 32 D antigen units of Type 3 poliovirus. For each lot of IPOL vaccine, D-antigen content is determined in vitro using the D-antigen ELISA assay. IPOL vaccine is produced from vaccine concentrates diluted with M-199 medium. Also present are 0.5% of 2-phenoxyethanol and a maximum of 0.02% of formaldehyde per dose as preservatives. Neomycin, streptomycin, and polymyxin B are used in vaccine production; and, although purification procedures eliminate measurable amounts, less than 5 ng neomycin, 200 ng streptomycin, and 25 ng polymyxin B per dose may still be present. The residual calf bovine serum albumin is less than 50 ng/dose in the final vaccine. The vaccine is clear and colorless and should be administered intramuscularly or subcutaneously. The vial stopper is not made with natural rubber latex.

**CLINICAL PHARMACOLOGY**

Polioviruses is caused by poliovirus Types 1, 2, or 3. It is primarily spread by the fecal-oral route of transmission but may also be spread by the pharyngeal route. Approximately 90% to 95% of poliovirus infections are asymptomatic. Nonspecific illness with low-grade fever and sore throat (minor illness) occurs in 4% to 8% of infections. Aspetic meningitis occurs in 1% to 5% of patients a few days after the minor illness has resolved. Rapid onset of asymmetric acute flaccid paralysis occurs in 0.1% to 2% of infections, and residual paralytic disease involving motor neurons (paralytic poliomyelitis) occurs in approximately 1 per 1,000 cases. (5)

Prior to the introduction of inactivated poliovirus vaccines in 1955, large outbreaks of poliomyelitis occurred each year in the United States (US). The annual incidence of paralytic disease of 11.4 cases/100,000 population declined to 0.5 cases by the time oral poliovirus vaccine (OPV) was introduced in 1961. Incidence continued to decline thereafter to a rate of 0.002 to 0.005 cases per 100,000 population. Of the 127 cases of paralytic poliomyelitis reported in the US between 1980 and 1994, six were imported cases (caused by wild polioviruses), two were “indeterminate” cases, and 119 were vaccine associated paralytic poliomyelitis (VAPP) cases associated with the use of live, attenuated oral poliovirus vaccine (OPV). (6) An all IPV schedule was adopted in 1999 to eliminate VAPP cases. (7)

**STUDY 1 (11)**

In one study, (13) the persistence of DA in infants receiving two doses of IPOL vaccine at 2 and 4 months of age was 91% to 100% (Type 1), 97% to 100% (Type 2), and 93% to 94% (Type 3) at twelve months of age. In another study, (12) 86% to 100% (Type 1), 95% to 100% (Type 2), and 82% to 94% (Type 3) of infants still had DA at 18 months of age. In trials and field studies conducted outside the US, IPOL vaccine, or a combination vaccine containing IPOL vaccine and DTP, was administered to more than 700 infants between 2 to 18 months of age manufactured by the same process as IPOL vaccine in primary monkey kidney cells have shown a direct relationship exists between the antigenic content of the vaccine, the frequency of seroconversion, and resulting antibody titer. Approval in the US was based upon demonstration of Immunogenicity and safety in US children. (11)

In the US, 219 infants received three doses of a similar enhanced IPV at two, four, and eighteen months of age manufactured by the same process as IPOL vaccine except the cell substrate for IPV was using primary monkey kidney cells. Seroversion to all three types of polioviruses was demonstrated in 99% of these infants after two doses of vaccine given at 2 and 4 months of age. Following the third dose of vaccine at 18 months of age, neutralizing antibodies were present at a level of ≥110 in 99.1% of children to Type 1 and 100% of children to Types 2 and 3 polioviruses. (3)

**STUDY 2 (12)**

In infants immunized with three doses of an unlicensed combination vaccine containing IPOL vaccine and DTP given during the first year of life, and a fourth dose given during the second year of life, the persistence of detectable neutralizing antibodies (DA) at ≥14 dilution were 95% to 100% (Type 1); 97% to 100% (Type 2) and 96% to 100% (Type 3) after two doses of IPV vaccine depending on studies. In infants immunized with three doses of an unlicensed combination vaccine containing IPV vaccine only schedules and sequential IPV-OPV schedules. (12) (13) Sero prevalences for detectable serum neutralizing antibody (DA) at ≥14 dilution were 95% to 100% (Type 1); 97% to 100% (Type 2) and 96% to 100% (Type 3) after two doses of IPV vaccine depending on studies.

<table>
<thead>
<tr>
<th>Age (months) for POST Dose 2</th>
<th>POST Dose 2</th>
<th>POST Dose 3</th>
<th>Pre Booster</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post Dose 2</td>
<td>Type 1</td>
<td>Type 2</td>
<td>Type 3</td>
</tr>
<tr>
<td>2 4 6 12 to 18 18</td>
<td>N'</td>
<td>%DA</td>
<td>%DA</td>
</tr>
</tbody>
</table>

**STUDY 3 (13)**

In infants immunized with three doses of an unlicensed combination vaccine containing IPV vaccine only schedules and sequential IPV-OPV schedules. (12) (13) Sero prevalences for detectable serum neutralizing antibody (DA) at ≥14 dilution were 95% to 100% (Type 1); 97% to 100% (Type 2) and 96% to 100% (Type 3) after two doses of IPV vaccine depending on studies.
Swedish IPV only schedule demonstrated persistence of detectable serum neutralizing antibody for at least 10 years in all three types of poliovirus. (15) IPV is able to induce secretory antibody (IgA) produced in the pharynx and gut and reduces pharyngeal excretion of poliovirus Type 1 from 75% in children with neutralizing antibodies at levels less than 1:8 to 25% in children with neutralizing antibodies at levels more than 1:64. (4) (14) (16) (17) (18) (19) (20) (21) (22) There is also evidence of induction of herd immunity with IPV, (15) (23) (24) (25) (26) and that this herd immunity is sufficiently maintained in a population vaccinated only with IPV. (26) VAPP has not been reported in association with administration of IPV vaccine. (27) It is expected that an IPV only schedule will eliminate the risk of VAPP in both recipients and contacts compared to a schedule that included OPV. (7)

INDICATIONS AND USAGE
IPOL vaccine is indicated for active immunization of infants (as young as 6 weeks of age), children, and adults for the prevention of poliomyelitis caused by poliovirus Types 1, 2, and 3. (28)

INFANTS, CHILDREN AND ADOLESCENTS
General Recommendations
It is recommended that all infants (as young as 6 weeks of age), unimmunized children, and adolescents not previously immunized be vaccinated routinely against paralytic poliomyelitis. (29) Following the eradication of poliomyelitis caused by wild poliovirus from the Western Hemisphere (including North and South America) (30), an IPV-only schedule was recommended to eliminate VAPP. (7)

All children should receive four doses of IPV at ages 2, 4, 6 to 18 months, and 4 to 6 years. OPV is no longer available in the US and is not recommended for routine immunization. (7)

Previous clinical poliomyelitis (usually due to only a single poliovirus type) or incomplete immunization with OPV are not contraindications to completing the primary series of immunization with IPOL vaccine. Children Incompletely Immunized
Children of all ages should have their immunization status reviewed and be considered for supplemental immunization as follows for adults. Time intervals between doses longer than those recommended for routine primary immunization do not necessitate additional doses as long as a final total of four doses is reached (see DOSAGE AND ADMINISTRATION section).

ADULTS
General Recommendations
Routine primary poliovirus vaccination of adults (generally those 18 years of age or older) residing in the US is not recommended. Unimmunized adults who are potentially exposed to wild polio and who have not been adequately immunized should receive polio vaccination in accordance with the schedule given in the DOSAGE AND ADMINISTRATION section. (28)

Persons with previous wild poliovirus disease who are incompletely immunized or unimmunized should be given additional doses of IPV vaccine if they fall into one or more categories listed. The following categories of adults are at an increased risk of exposure to wild polioviruses: (28) (31)

- Travelers to regions or countries where poliomyelitis is endemic or epidemic
- Healthcare workers in close contact with patients who may be excreting polioviruses
- Laboratory workers handling specimens that may contain polioviruses
- Members of communities or specific population groups with disease caused by wild polioviruses

IMMUNODEFICIENCY AND ALTERED IMMUNE STATUS
IPOL vaccine should be used in all patients with immunodeficiency diseases and members of such patients’ households when vaccination of such persons is indicated. This includes patients with asymptomatic HIV infection, AIDS or AIDS-Related Complex, severe combined immunodeficiency, hypogammaglobulinemia, or agammaglobulinemia; altered immune states due to diseases such as leukemia, lymphoma, or generalized malignancy; or an immune system compromised by treatment with corticosteroids, alkylating drugs, antimetabolites or radiation. Immunogenicity of IPOL vaccine in individuals infected with HIV, leukemia, or lymphoma could be impaired, and patients with an impaired immune state may or may not develop a protective response against paralytic poliomyelitis after administration of IPV. (32)

As with any vaccine, vaccination with IPOL vaccine may not protect 100% of individuals. Use with other vaccines: refer to DOSAGE AND ADMINISTRATION section for this information.

CONTRAINDICATIONS
IPOL vaccine is contraindicated in persons with a history of hypersensitivity to any component of the vaccine, including 2-phenoxyethanol, formaldehyde, neomycin, streptomycin, and polysorbate B. No further doses should be given if anaphylaxis or anaphylactic shock occurs within 24 hours of administration of one dose of vaccine. Vaccination of persons with an acute, febrile illness should be deferred until after recovery; however, minor illness, such as mild upper respiratory infection, with or without low grade fever, are not reasons for postponing vaccine administration.

WARNINGS
Neomycin, streptomycin, polysorbate B, 2-phenoxyethanol, and formaldehyde are used in the production of this vaccine. Although purification procedures eliminate measurable amounts of these substances, traces may be present (see DESCRIPTION section), and allergic reactions may occur in persons sensitive to these substances (see CONTRAINDICATIONS section).

Systemic adverse reactions reported in infants receiving IPV concomitantly at separate sites or combined with DTP have been similar to those associated with administration of DTP alone. (11) Local reactions are usually mild and transient in nature. Although no causal relationship between IPOL vaccine and Guillain-Barré Syndrome (GBS) has been established, (28) GBS has been temporally related to administration of another inactivated poliovirus vaccine. Deaths have been reported in temporal association with the administration of IPV (see ADVERSE REACTIONS section).

PRECAUTIONS
GENERAL
Prior to an injection of any vaccine, all known precautions should be taken to prevent adverse reactions. This includes a review of the patient’s history with respect to possible sensitivity to the vaccine or similar vaccines.

Healthcare providers should question the patient, parent or guardian about reactions to a previous dose of this product, or similar product. Epinephrine injection (1:1000) and other appropriate agents should be available to control immediate allergic reactions.

Healthcare providers should obtain the previous immunization history of the vaccinee, and inquire about the current health status of the vaccinee.

Immunodeficient patients or patients under immunosuppressive therapy may not develop a protective immune response against paralytic poliomyelitis after administration of IPV. Administration of IPOL vaccine is contraindicated in patients infected with HIV. (33) (34) (35) Special care should be taken to ensure that the injection does not enter a blood vessel.

INFORMATION FOR PATIENTS
Patients, parents, or guardians should be instructed to report any serious adverse reactions to their healthcare provider.

The healthcare provider should inform the patient, parent, or guardian of the benefits and risks of the vaccine.

The healthcare provider should inform the patient, parent, or guardian of the importance of completing the immunization series.

The healthcare provider should provide the Vaccine Information Statements (VISs) which are required to be given with each immunization.

DRUG INTERACTIONS
There are no known interactions of IPOL vaccine with drugs or foods. Concomitant administration of other parenteral vaccines, with separate syringes at separate sites, is not contraindicated. The first two doses of IPOL vaccine may be administered at separate sites using separate syringes concomitantly with DTP, acellular pertussis, Haemophilus influenzae type b (Hib), and hepatitis B vaccines. From historical data on the antibody responses to diphtheria, tetanus, acellular pertussis, Hib, or hepatitis B vaccines used concomitantly or in combination with IPOL vaccine, no interferences have been observed on the immunological end points accepted for clinical protection. (11) (16) (36) (See DOSAGE AND ADMINISTRATION section.)

If IPOL vaccine has been administered to persons receiving immunosuppressive therapy, an adequate safety and effectiveness evaluation will be conducted.

PREGNANCY
Animal reproduction studies have not been conducted with IPOL vaccine. It is also not known whether IPOL vaccine can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. IPOL vaccine should be given to a pregnant woman only if clearly needed.

NURSING MOTHERS
It is not known whether IPOL vaccine is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when IPOL vaccine is administered to a nursing woman.

PEDEATRIC USE
SAFETY AND EFFECTIVENESS OF IPOL VACCINE IN INFANTS BELOW SIX WEEKS OF AGE HAVE NOT BEEN ESTABLISHED. (12) (20) (See DOSAGE AND ADMINISTRATION section.)

In the US, infants receiving two doses of IPV at 2 and 4 months of age, the seroprevalence to all three types of poliovirus was demonstrated in 95% to 100% of these infants after two doses of vaccine. (12)

ADVERSE REACTIONS
Body System As A Whole
In earlier studies with the vaccine given in primary monkey kidney cells, transient local reactions at the site of injection were observed. (3) Erythema, induration and pain occurred in 3.2%, 1% and 13%, respectively, of vaccinees within 48 hours post-vaccination. Temperatures of ≥38°C (≥102°F) were reported in 36% of vaccinees. Other symptoms included irritability, sleepiness, fussiness, and crying. Because IPV was given in a different site but concurrently with Diphtheria and Tetanus Toxoids and Pertussis Vaccine Adsorbed (DTP), these systemic reactions could not be attributed to a specific vaccine. However, these systemic reactions were comparable in frequency and severity to that reported for DTP given alone without IPV. (12) Although no causal relationship has been established, deaths have occurred in temporal association after vaccination of infants with IPV. (37)

Four additional US studies using IPV vaccine in more than 1,300 infants, (12) between 2 to 18 months of age administered with DTP at the same time at separate sites or combined have demonstrated that local and systemic reactions were similar when DTP was given alone.

Table 2 (12): Percentage of Infants Presenting with Local or Systemic Reactions at 6, 24, and 48 Hours of Immunization with IPOL Vaccine Administered Intramuscularly Concomitantly at Separate Sites with Sanofi-Aventis Whole-Cell DTP Vaccine at 2 and 4 Months of Age and with Sanofi Aventis Pertussis Vaccine (Tripedia®) at 18 Months of Age

<table>
<thead>
<tr>
<th>REACTION</th>
<th>2 Months (n=211)</th>
<th>4 Months (n=200)</th>
<th>18 Months (n=74)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>6 Hrs.</td>
<td>24 Hrs.</td>
<td>48 Hrs.</td>
</tr>
<tr>
<td>Local, IPOL vaccine alone</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erythema &gt;1&quot;</td>
<td>0.5%</td>
<td>0.5%</td>
<td>0.5%</td>
</tr>
<tr>
<td>Swelling</td>
<td>11.4%</td>
<td>5.7%</td>
<td>0.9%</td>
</tr>
<tr>
<td>Tenderness</td>
<td>29.4%</td>
<td>8.5%</td>
<td>2.8%</td>
</tr>
</tbody>
</table>
Table 2 (12): Percentage of Infants Presenting with Local or Systemic Reactions at 6, 24, and 48 Hours of Immunization with IPOL Vaccine Administered Intramuscularly Concomitantly at Separate Sites with Sanofi Whole-Cell DTP Vaccine at 2 and 4 Months of Age and with Sanofi Acellular Pertussis Vaccine (Tripedia®) at 18 Months of Age (continued)

<table>
<thead>
<tr>
<th>AGE AT IMMUNIZATION</th>
<th>2 Months (n=211)</th>
<th>4 Months (n=206)</th>
<th>18 Months1 (n=74)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>6 Hrs. 24 Hrs. 48 Hrs.</td>
<td>6 Hrs. 24 Hrs. 48 Hrs.</td>
<td>6 Hrs. 24 Hrs. 48 Hrs.</td>
</tr>
<tr>
<td>Systemic5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fever &gt;102.2°F†</td>
<td>1.0% 0.5% 0.5%</td>
<td>2.0% 0.5% 0.0%</td>
<td>0.0% 0.0% 4.2%</td>
</tr>
<tr>
<td>Iritability</td>
<td>64.5% 24.6% 17.5%</td>
<td>49.5% 25.7% 11.7%</td>
<td>14.7% 6.7% 8.0%</td>
</tr>
<tr>
<td>Tiredness</td>
<td>60.7% 31.8% 7.1%</td>
<td>38.6% 18.4% 6.3%</td>
<td>9.3% 5.3% 4.0%</td>
</tr>
<tr>
<td>Anorexia</td>
<td>16.6% 8.1% 4.3%</td>
<td>6.3% 4.4% 2.4%</td>
<td>2.7% 1.3% 2.7%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1.9% 2.9% 2.8%</td>
<td>1.9% 1.5% 1.0%</td>
<td>1.3% 1.3% 0.0%</td>
</tr>
<tr>
<td>Persistent Crying</td>
<td>Percentage of infants within 72 hours after immunization was 0.0% after dose one, 1.4% after dose two, and 0.0% after dose three.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

†Children who have been vaccinated with Tripedia vaccine. 
‡Data from the IPOL vaccine administration site, given intramuscularly. 
§The adverse reaction profile includes the concomitant use of Sanofi whole-cell DTP vaccine or Tripedia vaccine with IPOL vaccine. Rates are comparable in frequency and severity to that reported for whole-cell DTP given alone. 

Dose of Immunization

The primary series of IPOL vaccine consists of three 0.5 mL doses administered intramuscularly or subcutaneously, preferably eight or more weeks apart and usually at ages 2, 4, and 6 to 18 months. Under no circumstances should the vaccine be given more frequently than four weeks apart. The first immunization may be administered as early as six weeks of age. For this series, a booster dose of IPOL vaccine is administered at 4 to 6 years of age. (41)

Use of Other Vaccines

From historical data on the antibody responses to diphtheria, tetanus, whole-cell or acellular pertussis, Hib, or hepatitis B vaccines used concomitantly with IPOL vaccine, no interferences have been observed on the immunological end points accepted for clinical protection. (11) (16) (36) (See DRUG INTERACTIONS section). If the third dose of IPOL vaccine is given between 12 to 18 months of age, it may be desirable to administer this dose with Measles, Mumps, and Rubella (MMR) vaccine and/or other vaccines using separate syringes at separate sites, (28) but no data on the immunological interference between IPOL vaccine and these vaccines exist.

Use in Previously Vaccinated Children

Children and adolescents with a previously incomplete series of polio vaccine should receive sufficient additional doses of IPOL vaccine to complete the series. Interruption of the recommended schedule with a delay between doses does not interfere with the final immunity. There is no need to start the series over again, regardless of the time elapsed between doses. The need to routinely administer additional doses is unknown at this time. (28)

Adults

Unvaccinated Adults

A primary series of IPOL vaccine is recommended for unvaccinated adults at increased risk of exposure to poliovirus. While the responses of adults to primary series have not been studied, the recommended schedule for adults is two 0.5 mL doses given at 1 to 2 month interval and a third 0.5 mL dose given 6 to 12 months later. If less than 3 months but more than 2 months are available before protection is needed, three doses of IPOL vaccine should be given at least 1 month apart. Likewise, if only 1 or 2 months are available, two 0.5 mL doses of IPOL vaccine should be given at least 1 month apart. If less than 1 month is available, a single 0.5 mL dose of IPOL vaccine is recommended. (28)

Incompletely Vaccinated Adults

Adults who are at an increased risk of exposure to poliovirus and who have had at least one dose of OPV, fewer than three doses of conventional IPV or a combination of conventional IPV or OPV totaling fewer than three doses should receive at least one 0.5 mL dose of IPOL vaccine. Additional doses needed to complete a primary series should be given if time permits. (28)

Completely Vaccinated Adults

Adults who are at an increased risk of exposure to poliovirus and who have previously completed a primary series with one or a combination of polo vaccines can be given a 0.5 mL dose of IPOL vaccine. The preferred injection site of IPOL vaccine for adults is in the deltoid area.

HOW SUPPLIED

Multi-dose vial , 5mL: NDC 42821-860-78. Supplied as package: NDC 42821-860-10.

STORAGE

The vaccine is stable if stored in the refrigerator at 2°C to 8°C (35°F to 46°F). The vaccine must not be frozen. Protect from light.

REFERENCES

11. Unpublished data available from Sanofi Pasteur SA.
12. Unpublished data available from Sanofi Pasteur Inc.


Product Information as of May 2020

Manufactured by:
Sanofi Pasteur SA
Marcy L’Etoile France
US Govt License #1724

Distributed by:
Sanofi Pasteur Inc.
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POL-FSPL-SL-MAY20