PRODUCT MONOGRAPH

INACTIVATED POLIOMYELITIS VACCINE
(DIPLOID CELL ORIGIN) - IPV

Dosage Form: Solution for Injection
Single Dose Ampoule

Active Immunizing Agent
(For the Prevention of Poliomyelitis)

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ACTION AND CLINICAL PHARMACOLOGY

Poliomyelitis is a disease that may cause irreversible paralysis in a certain proportion of infected individuals. It is a highly infectious disease caused by three types of the enterovirus poliovirus. (1) It is primarily spread by the fecal-oral route of transmission but may also be spread by the pharyngeal route. Following introduction of poliovirus vaccine in Canada in 1955, indigenous disease has been virtually eliminated.

The last significant outbreak of poliomyelitis occurred in 1978-79, when there were 11 cases of paralytic disease among unimmunized contacts of imported cases. The last case of poliomyelitis attributed to imported, wild virus occurred in 1988. (1) However, circulation of wild viruses does occur in rare circumstances (2), and it remains crucial that the highest possible level of vaccine-induced immunity be maintained in the population. Inactivated Poliomyelitis Vaccine (Diploid Cell Origin) - IPV, (sometimes referred to as e-IPV), is an enhanced formalin-inactivated product which has a higher potency than the original IPV. The three poliovirus types are propagated in human diploid cells. A primary series induces protective antibody levels in more than 99% of recipients. (3)

The clinical data for Inactivated Poliomyelitis Vaccine (Diploid Cell Origin) - IPV were obtained from two centres: one in Canada (British Columbia) and the other in the U.S. (Baltimore, Maryland). Serum samples from both sites were tested for neutralizing antibody to poliovirus Types 1, 2 and 3 by the micrometabolic inhibition test at Sanofi Pasteur Limited.

The clinical trial data on three lots of Inactivated Poliomyelitis Vaccine (Diploid Cell Origin) - IPV obtained from a study on 338 infants in British Columbia demonstrated that two injections of vaccine at an interval of 2 months administered to infants 2 months of age at the time of the initial injection were effective in stimulating an antibody response to each of the three poliovirus types.

The response to Inactivated Poliomyelitis Vaccine (Diploid Cell Origin) - IPV developed despite the presence of maternally-transmitted antibody in most of the infants at the time of the initial vaccine injection. Following the second injection of vaccine, detectable antibody (≥1:4) was present in 99.7% (of 329 children) for Types 1 and 2 and in 98.8% (of 329 children) for Type 3.

In 294 children, the third vaccine injection at 15-18 months of age stimulated antibody rises to each of the three virus types to levels much higher than those attained following the second injection. The geometric mean responses 1 month after the third dose were 1:1922, 1:4010 and 1:1388 for poliovirus Types 1, 2 and 3, respectively.

The data obtained in the Baltimore trials in a group of 254 infants demonstrated that two injections of vaccine at an interval of 2 months administered to infants 2 months of age at the time of the initial injection were effective in stimulating an antibody response to each of the three poliovirus types. Following the second vaccine injection, detectable antibody (≥1:4) to Type 1 poliovirus was present in 98.8% of infants and antibody (≥1:4) to Types 2 and 3 poliovirus was present in 99.2% of infants.

The response to vaccine developed despite the presence of maternally-transmitted antibody in a high percentage of the infants at the time of the initial vaccine injection.

INDICATIONS AND CLINICAL USE

Inactivated Poliomyelitis Vaccine (Diploid Cell Origin) - IPV is indicated for active immunization against poliomyelitis caused by poliovirus types 1, 2 and 3 in infants, children and adults both for primary immunization and for boosters as described below.

Infants, Children and Adolescents

It is recommended that all infants, unimmunized children and adolescents not previously immunized be vaccinated routinely against paralytic poliomyelitis. (1) (4)

Incompletely Immunized Children

Children of all ages should have their immunization status reviewed and be considered for supplemental immunization. (See DOSAGE AND ADMINISTRATION.)

Adults

All adults at risk of exposure to poliovirus should have their immunization status reviewed. For those who are unvaccinated, who have a history of incomplete immunization, or for whom immunization is uncertain, a primary series of Inactivated Poliomyelitis Vaccine (Diploid Cell Origin) – IPV is recommended. (See DOSAGE AND ADMINISTRATION.) The following categories of persons are at increased risk of exposure to poliovirus: (1) (5)

- travellers to areas of countries where poliomyelitis is still transmitted, (6)
- laboratory workers handling specimens that may contain polioviruses,
- unimmunized parents or child care workers who will be caring for children in countries where OPV is used (1) or in rare instances in which infants receive OPV in a country that normally uses inactivated poliomyelitis,
- members of communities or specific population groups with disease caused by wild poliovirus. (7)

Inactivated Poliomyelitis Vaccine (Diploid Cell Origin) – IPV can be used for completing series of immunization in cases of previous clinical poliomyelitis (usually due to only a single poliovirus type) or incomplete immunization with OPV.

HIV-infected individuals, both asymptomatic and symptomatic, should be immunized with Inactivated Poliomyelitis Vaccine (Diploid Cell Origin) – IPV according to standard schedules. (1)

CONTRAINDICATIONS

Immunization with Inactivated Poliomyelitis Vaccine (Diploid Cell Origin) – IPV should be deferred in the presence of any acute illness, including febrile illness to avoid superimposing adverse effects from the vaccine on the underlying illness or mistakenly identifying a manifestation of the underlying illness as a complication of vaccine use. A minor illness such as mild upper respiratory infection is not reason to defer immunization. (1)

Allergy to any component of Inactivated Poliomyelitis Vaccine (Diploid Cell Origin) – IPV, or its container, or an anaphylactic or other allergic reaction to a previous dose of Inactivated Poliomyelitis Vaccine (Diploid Cell Origin) – IPV is a contraindication to vaccination. (See components listed in PHARMACEUTICAL INFORMATION, Composition.)

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

WARNINGS

Since the vaccine contains trace amounts of bovine serum albumin and may contain trace amounts of polymyxin B and neomycin, the possibility of allergic reactions in individuals sensitive to these substances should be borne in mind when considering the use of this vaccine.

Immunocompromised persons (whether from disease or treatment) may not obtain the expected immune response. If possible, consideration should be given to delaying vaccination until after the completion of any immunosuppressive treatment. (1)

As with any vaccine, immunization with Inactivated Poliomyelitis Vaccine (Diploid Cell Origin) - IPV may not protect 100% of susceptible individuals.

PRECAUTIONS

The possibility of allergic reactions in persons sensitive to components of the vaccine should be evaluated. Epinephrine Hydrochloride Solution (1:1,000) and other appropriate agents should be available for immediate use in case an anaphylactic or acute hypersensitivity reaction occurs. (1) Health-care providers should be familiar with current recommendations for the initial management of anaphylaxis in non-hospital settings, including proper airway management. (1) (8)

For instructions on recognition and treatment of anaphylactic reactions, see the current edition of the Canadian Immunization Guide or visit the Health Canada website.

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, the presence of any contraindications to immunization and current health status.

Before administration of Inactivated Poliomyelitis Vaccine (Diploid Cell Origin) - IPV health-care personnel should inform the parent or guardian or the patient to be immunized of the benefits and risks of immunization, inquire about the recent health status of the patient and comply with any local requirements with respect to information to be provided to the patient before immunization and the importance of completing the immunization series.

It is extremely 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. (See CONTRAINDICATIONS and ADVERSE REACTIONS.)

Do not inject into a blood vessel.

Aseptic technique must be used. Use a separate sterile needle and syringe, or a sterile disposable unit, for each individual patient to prevent disease transmission.

Administering the most widely used live and inactivated vaccines during the same patient visit has produced seroconversion rates and rates of adverse reactions similar to those observed when the vaccines are administered separately. (1) Simultaneous administration using separate syringes at separate sites is suggested, particularly when there is concern that an individual may not return for subsequent vaccination. Clinical trials have shown that IPV is safe and immunogenic if administered at the same time as DPT , Td, and DTaP (9); separate syringes are used for each vaccine and each vaccine is administered at separate sites.

Pregnancy and Lactation

No clinical trials with inactivated poliomyelitis vaccine have been conducted on pregnant women. Although there is no convincing evidence documenting adverse effects of inactivated poliomyelitis vaccine on the pregnant woman or the developing fetus, it is prudent on theoretical grounds to avoid vaccinating pregnant woman.

The National Advisory Committee on Immunization (NACI) states that IPV is not contraindicated in pregnancy, but its administration should be delayed until after the first trimester, if possible, to minimize any theoretical risk. If risk of exposure is imminent, IPV should be given and is always the vaccine of choice except for outbreak control. (1)

ADVERSE REACTIONS

Local reactivity at the injection site as observed during the Canadian clinical trials consisted of redness, hardness and pain or discomfort occurring in 14%, 4% and 12% of vaccinees respectively, usually on the evening following injection and declining thereafter to minimal levels.

As both of the first and second Inactivated Poliomyelitis Vaccine (Diploid Cell Origin) - IPV injections were administered at the same time, but at a different site from the first and second injections of Diphtheria and Tetanus Toxoids and Pertussis Vaccine Adsorbed (DPT Adsorbed), interpretation of systemic reactivity cannot be attributed solely to either vaccine. However, the

systemic reactivity associated with administration of DPT Adsorbed in previous clinical trials would tend to indicate that the DPT Adsorbed was the major contributory factor.

An extensive review by the US Institute of Medicine of adverse events associated with vaccination suggested that no serious adverse events have been associated with IPV. (7)

Physicians, nurses, and pharmacists should report any adverse occurrences temporally related to the administration of the product in accordance with local requirements and to the Global Pharmacovigilance Department, Sanofi Pasteur Limited, 1755 Steeles Avenue West, Toronto, ON, M2R 3T4, Canada. 1-888-621-1146 (phone) or 416-667-2435 (fax).

DOSAGE AND ADMINISTRATION

A primary series of Inactivated Poliomyelitis Vaccine (Diploid Cell Origin) - IPV consists of three 0.5 mL doses administered subcutaneously. The interval between the first two doses should be at least four weeks, but preferably eight weeks. The first two doses are usually integrated with DPT immunization and may be given at two and four months of age or at 4 and 6 months of age. The third dose should follow at least six months but preferably 12 months later.

Alternatively, three doses of 0.5 mL may be administered at intervals of 8 weeks, followed by a fourth dose of 0.5 mL approximately 12 months after the third dose. Although it is recommended that immunization be started at 2 months of age, if for any reason it is delayed, the same schedule may be used.

The primary schedule is usually integrated with combination infant vaccines against diphtheria, tetanus, pertussis and *Haemophilus influenzae* type b, beginning at 2 months of age.

Booster Doses

All children who received a primary series of Inactivated Poliomyelitis Vaccine (Diploid Cell Origin) – IPV, or a combination of IPV and OPV, should be given a booster dose at 4-6 years, unless the last dose of the primary series was administered on or after the fourth birthday. An additional booster dose should be given at age 14-16 years unless OPV was used exclusively

during the primary series. The need to administer additional doses routinely is unknown at this time.(4)

A final total of at least four doses is necessary to complete a series of primary and booster doses. Children and adolescents with a previously incomplete series of IPV should receive sufficient additional doses to reach this number.

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.

For children who began their polio immunization series in a country where OPV is used, immunization may be completed using IPV; there is no need to re-start the series. Conversely, children who have been started on an immunization series with IPV and who move to an area where OPV is used may receive the necessary doses of OPV to complete their series. (1)

ADULTS

For unimmunized adults at increased risk, primary immunization with IPV is recommended as two doses given at an interval of 4 to 8 weeks with a further dose 6 months to 1 year later.

Additional considerations are as follows:

- Travellers: travellers who will be departing in <4 weeks should receive a single dose of IPV and the remaining doses later, at the recommended intervals.(1)
- Unimmunized parents/child care workers: in those instances in which infants receive OPV, there is a very small risk of OPV-associated paralysis to unimmunized parents or to other household contacts. It will generally not be practical for such people to be fully protected with IPV before the infant is immunized; their risk may be reduced if they are given one dose of IPV at the same time as the first dose is given to the infant. Arrangements should be made for the adults to complete their basic course of immunization.(1)

- Incompletely immunized adults at increased risk (see INDICATIONS) who have previously received less than a full primary course of IPV or OPV should receive the remaining dose(s) of poliovirus vaccine as IPV, regardless of the interval since the last dose.(1)

For information on vaccine administration see the current edition of the Canadian Immunization Guide or visit the Health Canada website.

Inspect for extraneous particulate matter and/or discolouration before use. If these conditions exist, the product should not be administered.

SHAKE THE AMPOULE WELL to uniformly distribute the solution before withdrawing each dose. Before withdrawing a dose from an ampoule, tap the container first to ensure that any vaccine in the ampoule neck falls to the lower portion of the ampoule. Once the ampoule has been opened, any of its contents not used immediately should be discarded. Aseptic technique must be used for withdrawal of each dose.

Do not inject intravenously.

Needles should not be recapped and should be disposed of properly.

Give the patient a permanent personal immunization record. In addition, it is essential that the physician or nurse record the immunization history in the permanent medical record of each patient. This permanent office record should contain the name of the vaccine, date given, dose, manufacturer and lot number.

PHARMACEUTICAL INFORMATION

Composition

Inactivated Poliomyelitis Vaccine (Diploid Cell Origin) – IPV is a sterile suspension of three types of poliovirus: Type 1 (Mahoney), Type 2 (MEF-1) and Type 3 (Saukett). Inactivated Poliomyelitis Vaccine (Diploid Cell Origin) – IPV is a highly purified, inactivated poliovirus vaccine produced by microcarrier culture. (10) (11) The viruses are grown in cultures of MRC-5 cells, a line of normal human diploid cells, by the microcarrier technique. The cells are grown in CMRL 1969 medium, supplemented with calf serum. For viral growth the culture medium is replaced by M-199, without calf serum.

After clarification and filtration, viral suspensions are concentrated by ultrafiltration and purified. The monovalent viral suspensions are inactivated at 37°C with 1:4,000 formalin. Monovalent concentrates of each type are then combined to produce a trivalent concentrate.

Each dose (0.5 mL) contains:

poliovirus	Type 1 (Mahoney)	40 D antigen units
	Type 2 (MEF-1)	8 D antigen units
	Type 3 (Saukett)	32 D antigen units
formaldehyde		27 ppm
2-phenoxyethanol (not as a preservative)		0.5%
polymyxin B		trace amounts (<4 pg by calculation)
neomycin		trace amounts (<4 pg by calculation)
bovine serum albumin		≤50 ng*
polysorbate 80		approx. 20 ppm*
phosphate buffered saline		q.s. to 0.5 mL

* by calculation

The vaccine is clear and colourless and should be administered subcutaneously.

Stability and Storage

Store at 2° to 8°C (35° to 46°F). DO NOT FREEZE. Discard product if exposed to freezing.

Do not use after expiration date.

AVAILABILITY OF DOSAGE FORMS

5 x 0.5 mL ampoules

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Vaccine Information Service: 1-888-621-1146 or 416-667-2779.
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