

Td POLIO ADSORBED



Tetanus and Diphtheria Toxoids Adsorbed and Inactivated Poliomyelitis Vaccine

For 7 years and Older

DESCRIPTION

Td Polio Adsorbed - Tetanus and Diphtheria Toxoids Adsorbed and Inactivated Poliomyelitis Vaccine, as supplied by Aventis Pasteur Limited, is a sterile, cloudy, uniform suspension of tetanus and diphtheria toxoids adsorbed on aluminium phosphate and combined with Inactivated Poliomyelitis Vaccine.

Each dose (0.5 mL) contains:

purified inactivated poliomyelitis vaccine	Type 1 (Mahoney) Type 2 (M.E.F.1) Type 3 (Saukett)
tetanus toxoid	5 Lf
diphtheria toxoid	2 Lf
aluminum phosphate	1.5 mg
formaldehyde	27 ppm

Trace amounts of neomycin and polymyxin B may be present from the cell growth medium. 2-phenoxyethanol 0.5% is added as a preservative.

CLINICAL PHARMACOLOGY

Immunization against tetanus, diphtheria and polio has been associated with a striking decrease in the incidence of morbidity and mortality from these diseases. Simultaneous vaccination with combination vaccines containing diphtheria and tetanus toxoids and inactivated poliomyelitis vaccine has been a cornerstone of the Canadian immunization programme.

Tetanus is an acute and often fatal disease caused by an extremely potent neurotoxin produced by *Clostridium tetani*. The organism is ubiquitous and its occurrence in nature cannot be controlled. Immunization is highly effective, produces long-lasting protection, and is recommended for the whole population. Only 2 to 7 cases of tetanus are now reported annually in Canada.¹ Tetanus toxoid is prepared by detoxification of tetanus toxin with formaldehyde.

Diphtheria is a serious communicable disease caused by toxigenic strains of *Corynebacterium diphtheriae*. The organism may be harboured in the nasopharynx, skin or other sites of asymptomatic carriers, making eradication of the disease difficult. Routine immunization against diphtheria in infancy and childhood has been widely practiced in Canada since 1930, resulting in a decline in morbidity and mortality. Fewer than 5 cases are now reported annually in Canada and no deaths have been reported since 1983, however there is the potential for disease reemergence if immunization levels are allowed to fall and adults do not receive booster doses.¹ The disease occurs most frequently in unimmunized or partially immunized individuals.¹ Diphtheria toxoid is a cell-free preparation of diphtheria toxin detoxified with formaldehyde. The immunity conferred is antitoxic, not antibacterial, and thus protects against the potentially lethal systemic effects of diphtheria toxin but not directly against local infection.¹

Injection of bacterial proteins such as tetanus and diphtheria toxoids results in the production of protective antibodies. A primary series consisting of two or more injections is required to prime the immune system and produce a satisfactory protective antibody level. Tetanus antitoxin levels of >0.01 IU/mL are generally accepted as good evidence of immunity from tetanus. Diphtheria antitoxin levels of ≥ 0.01 IU/mL are thought to be the minimal level required for protection. Levels >0.05 IU/mL are considered optimal for protection.² After completion of a primary series, levels of circulating antibodies to tetanus and diphtheria toxoids decline gradually but are thought to persist at protective levels for up to 10 years.¹ Tetanus and Diphtheria toxoid boosters are recommended every 10 years.

Poliomyelitis is caused by infection with one of three antigenic types of poliovirus. Following introduction of poliovirus vaccine in Canada in 1955, the indigenous disease has been virtually eliminated. The last significant outbreak of poliomyelitis occurred in 1978-1979, 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,³ and it remains crucial that the highest possible level of vaccine-induced immunity be maintained in the population.

In 1993, 22 asymptomatic cases of imported wild polio infection were documented, and importation of wild virus was documented in an asymptomatic child in 1996.¹ Further spread of the virus was not seen, presumably because of high levels of immunization in the rest of 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.⁴

Clinical Trial Data:

In a clinical trial involving 276 individuals previously immunized against tetanus, diphtheria and poliomyelitis, a single (0.5 mL) injection of Td Polio Adsorbed - Tetanus and Diphtheria Toxoids Adsorbed and Inactivated Poliomyelitis Vaccine, of any of the three vaccine lots tested, stimulated a prompt antibody response to each of the antigens - tetanus, diphtheria and poliovirus types 1, 2, and 3.⁴

Antibody Titres in Recipients of a Single (0.5 mL) Injection of Td Polio Adsorbed

	PRE-INJECTION		28 DAYS POST INJECTION	
	Range	G.M.T.*	Range	G.M.T.*
Tetanus Antitoxin IU/mL	0.01-14.0	0.72	0.56-14.0	2.78
Diphtheria Antitoxin IU/mL	0.005-10.24	0.17	0.04-40.96	1.34
Poliovirus Neutralizing Antibody				
Type 1	1:4-1:2048	1:69.8	1:8-1:16384	1:383.9
Type 2	1:4-1:2048	1:67.2	1:16-1:16384	1:573.0
Type 3	1:4-1:2048	1:44.4	1:16-1:32768	1:1007.4

* G.M.T. = Geometric Mean Titre

Response to the reinforcement injection was equally satisfactory in those whose most recent previous injection had been received more than 10 years previously as in those with a shorter interval since the last previous injection.⁴

The immunogenicity of the tetanus and diphtheria components of Td Polio Adsorbed administered as a series of three (0.5 mL) injections for primary immunization has been demonstrated in a small number (17) of individuals whose ages ranged from 6 to 56 years. These individuals were all confirmed unimmunized to both tetanus and diphtheria. Four weeks following the second injection of vaccine, given two months after the first, all had responded with serum tetanus antitoxin levels ranging from 0.11 to 14.0 IU/mL and with diphtheria antitoxin levels ranging from

0.01 to 1.28 IU/mL. Following the third injection of vaccine 6 to 8 months after second, the 8 individuals tested developed antitoxin titres to tetanus of 0.56 to 14.0 IU/mL and to diphtheria of 0.16 to 5.12 IU/mL.⁴

Inclusion of inactivated poliomyelitis vaccine with the tetanus and diphtheria toxoids adsorbed and the spacing of the three injections at 0, 2 and 6-12 months, produced an adequate neutralizing antibody response to all three types of poliovirus.⁴

INDICATIONS

Td Polio Adsorbed - Tetanus and Diphtheria Toxoids Adsorbed and Inactivated Poliomyelitis Vaccine is indicated for secondary immunization **in children aged 7 years and older and adults who have been previously immunized against tetanus, diphtheria and poliomyelitis.**

Td Polio Adsorbed may also be used for primary immunization of older children (7 years of age and over) and of adults who have not been immunized previously against tetanus, diphtheria and poliomyelitis.

Persons who have had tetanus or diphtheria should still be immunized since these clinical infections do not always confer immunity.¹ Persons who have had poliomyelitis may receive IPV, as they may not be fully protected against all 3 poliovirus serotypes.

Human Immunodeficiency Virus (HIV) Infected Persons

HIV-infected individuals, both asymptomatic and symptomatic, should be immunized against tetanus, diphtheria and poliomyelitis according to standard schedules.¹

CONTRAINDICATIONS

General

Immunization with Td Polio Adsorbed - Tetanus and Diphtheria Toxoids Adsorbed and Inactivated Poliomyelitis Vaccine, 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 attributing to the vaccine a manifestation of the underlying illness. A minor afebrile illness such as mild upper respiratory infection is not usually reason to defer immunization.¹

Absolute Contraindications

Allergy to any component of Td Polio Adsorbed (see components listed in DESCRIPTION) or an anaphylactic or other allergic reaction to a previous dose of Td Polio Adsorbed are contraindications to vaccination.

Elective immunization of persons over 6 months of age should be deferred during an outbreak of poliomyelitis because of the risk of provocation paralysis.^{5,6}

WARNINGS

Intramuscular injections should be given with care in persons suffering from coagulation disorders or on anticoagulant therapy because of the risk of hemorrhage.¹

If Td Polio Adsorbed - Tetanus and Diphtheria Toxoids Adsorbed and Inactivated Poliomyelitis Vaccine is used in persons with malignancies, persons receiving immunosuppressive therapies, including irradiation, antimetabolites, alkylating agents, cytotoxic drugs, or persons who are otherwise immunocompromised (including HIV infected individuals, transplant recipients, persons suffering from autoimmune disorders), the expected immune response may not be obtained.

Corticosteroid therapy can result in immunosuppression although the exact dose and duration of therapy required to suppress the immune system is not well defined. Persons treated with high doses of systemic steroids,

e.g., ≥ 2 mg/kg/day of prednisone orally for more than 2 weeks or ≥ 60 mg prednisone/day in an adult, should be considered to have a compromised immune system.⁷

As with any vaccine, immunization with Td Polio Adsorbed may not protect 100% of susceptible individuals.

PRECAUTIONS

General

The possibility of allergic reactions in individuals sensitive to components of the vaccine should be evaluated. Epinephrine Hydrochloride Solution (1:1000) 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}

Before administration of any vaccine, all appropriate precautions should be taken to prevent adverse reactions. This includes a review of the patient's history with respect to possible hypersensitivity to the vaccine or similar vaccine, determination of previous immunization history, and the presence of any contraindications to immunization, current health status, and knowledge of the current literature concerning the use of the vaccine under consideration.

Frequent booster doses of tetanus or diphtheria toxoids in the presence of adequate or excessive serum levels of tetanus or diphtheria antitoxins have been associated with increased incidence and severity of reactions and should be avoided. If hypersensitivity to the diphtheria component is suspected, tetanus toxoid should be used for reinforcing doses.

Special care should be taken to ensure that the product is not injected into a blood vessel (see DOSAGE AND ADMINISTRATION).

Caution

A separate sterile needle and syringe, or a sterile disposable unit, must be used for each individual patient to prevent the transmission of infectious agents.

There have been case reports of transmission of HIV and hepatitis by failure to scrupulously observe sterile technique. In particular, the same needle and/or syringe must never be used to re-enter a multi-dose vial to withdraw vaccine even when it is to be used for inoculation of the same patient. This may lead to contamination of the vial contents and infection of patients who subsequently receive vaccine from the vial.⁹

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

Before administration of Td Polio Adsorbed - Tetanus and Diphtheria Toxoids Adsorbed and Inactivated Poliomyelitis Vaccine, healthcare personnel should inform the patient or parent or guardian of 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.

ADVERSE REACTIONS

During the clinical trial of Td Polio Adsorbed - Tetanus and Diphtheria Toxoids Adsorbed and Inactivated Poliomyelitis Vaccine, the vaccinees experienced only a low level of reactions associated with the injections. Discomfort at the injection site was usually of short duration. Systemic complaints included mild fever (none exceeded 37.6°C), headache, malaise, tiredness and dizziness. No side effects of major significance were noted.⁴

Localized reactions consisting of discomfort, pain, swelling and redness at the injection site may be associated with tetanus and diphtheria toxoids.^{7,10} These are usually of low frequency and transient in duration. Following booster

doses, local erythema and swelling are not uncommon and Arthus-type sensitivity may occur.¹ Severe local reactions are often associated with high levels of circulating antitoxin, usually resulting from over-immunization due to toxoid being given too frequently.^{1,11,12} Systemic reactions, such as generalized urticaria, are uncommon. Influenza-like symptoms have been reported and usually occur within 12 hours of vaccination with some tetanus and diphtheria toxoids.¹⁰

Neurological complications such as peripheral neuropathies^{13,14} demyelinating diseases of the central nervous system (CNS)¹⁵ following tetanus toxoid or diphtheria toxoid have been documented but are rare.¹⁶ The US Institute of Medicine has concluded that the evidence is inadequate to accept or reject a causal relation between tetanus toxoid, DT or Td and demyelinating diseases of the CNS (acute demyelinating encephalomyelitis, transverse myelitis, optic neuritis) or peripheral mononeuropathy (other than those caused by direct intraneural injection).¹⁵

The following neurologic illnesses have been reported as temporally associated with some vaccines containing tetanus toxoid: neurological complications¹⁷ including cochlear lesion,¹⁸ brachial plexus neuropathies,^{13,18} paralysis of the radial nerve¹⁴ paralysis of the recurrent nerve,¹⁸ accommodation paresis, and EEG disturbances with encephalopathy (with or without permanent intellectual and/or motor function impairment).¹⁹ Reports of these are rare. In the differential diagnosis of polyradiculoneuropathies following administration of a vaccine containing tetanus toxoid, tetanus toxoid should be considered as a possible etiology.^{15,20} The Institute of Medicine concluded that the evidence favours acceptance of a causal relation between tetanus toxoid and brachial neuritis.¹⁵

On the basis of one case report and evidence that a vaccine-induced immunologic response can cause Guillain Barré Syndrome (GBS), the Institute of Medicine concluded that tetanus toxoid-containing vaccines can trigger GBS in adults. No increased risk for GBS has been observed with the use of DTP in children.¹⁶

Persistent nodules at the site of injection have occurred following the use of an adsorbed product, but this complication is unusual²¹ and may be related to subcutaneous administration.⁸ Sterile abscess at the site of injection has been reported following use of adsorbed vaccines (6-10 per million doses).²²

Rare cases of allergic or anaphylactic reaction (i.e., hives, swelling of the mouth, difficulty breathing, hypotension, or shock) have been reported after receiving some preparations containing diphtheria, tetanus and/or poliomyelitis antigens.²² Death following vaccine-caused anaphylaxis has been reported.¹⁵

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 Medical Director at Aventis Pasteur Limited, 1755 Steeles Avenue West, Toronto, Ontario, Canada M2R 3T4.

DOSAGE AND ADMINISTRATION

For persons who have previously been immunized against tetanus, diphtheria and poliomyelitis, a dose of 0.5 mL should be administered as a reinforcing dose at approximately 10 year intervals.

When travel to a developing country is planned more than 5 years after the last tetanus booster, it may be prudent to offer an early booster, since in some developing countries health care facilities may not be able to guarantee the safe administration of a booster dose if required.¹

For primary immunization of persons aged 7 years and older a series of three (0.5 mL) doses is required. The first two doses should be given 2 months apart and the third dose 6 to 12 months later.^{1,8,22,23} The National Advisory Committee on Immunization states that the first 2 doses should be given 4 - 8 weeks apart.

Tetanus Prophylaxis in Wound Management¹

The following table summarizes the recommended use of immunizing agents in wound management. It is important to ascertain the number of doses of tetanus toxoid previously given and the interval since the last dose. If not clearly documented, a history of immunization should be regarded as "uncertain". When a tetanus booster is required a combined preparation formulated for adults including tetanus and diphtheria toxoid is preferable (i.e. Td ADSORBED). Appropriate cleansing and debridement of the wound is imperative. Booster doses given more frequently than recommended below may lead to local and systemic adverse reactions.

History of tetanus	Clean, minor wounds		All other wounds	
	Td Polio*	TIG†	Td Polio	TIG
Uncertain or primary** immunization incomplete	Yes	No	Yes	Yes
Primary** immunization complete	Yes‡	No	Yes§	No¶

* Adult type tetanus and diphtheria toxoids and poliomyelitis vaccine (for 7 years and older). If the patient is < 7 years old, an appropriate tetanus combination vaccine such as TRIPACEL™ or PENTACEL™ is given.

** Primary immunization is at least 3 doses at age appropriate intervals.

† Tetanus immune globulin.

‡ Yes, unless there is documentation of a booster within the last 10 years.

§ Yes, unless there is documentation of a booster within the last 5 years.

¶ No, unless individuals are known to have a significant immune deficiency state (e.g., HIV, ammaglobulinemia) since immune response to tetanus toxoid may be suboptimal.

NOTE: Diphtheria and Tetanus Toxoids Adsorbed and Poliomyelitis Vaccine, containing 25 Lf of diphtheria toxoid and 5 Lf of the tetanus toxoid per 0.5 mL dose, should not be administered as a tetanus booster to children aged 7 years and older or adults due to the higher diphtheria toxoid component in this vaccine.

NOTE: Tetanus toxoid, or a multi-valent vaccine containing tetanus toxoid, and tetanus immune globulin should be administered in separate syringes at different sites.

Parenteral biological products should be inspected visually for extraneous particulate matter and/or discoloration before administration. If these conditions exist, the product should not be administered.

SHAKE THE VIAL OR AMPOULE WELL to distribute uniformly the suspension 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. When administering a dose from a rubber-stoppered vial, do not remove either the rubber stopper or the metal seal holding it in place. Aseptic technique must be used for withdrawal of each dose (see PRECAUTIONS).

Before injection, the skin over the site to be injected should be cleansed with a suitable germicide.

Administer the vaccine **intramuscularly**. The preferred site is into the deltoid muscle.

After insertion of the needle, aspirate to ensure that the needle has not entered a blood vessel.

DO NOT INJECT INTRAVENOUSLY.

Each person who is immunized should be given 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, route of administration, manufacturer and lot number.

STORAGE

Td Polio Adsorbed - Tetanus and Diphtheria Toxoids Adsorbed and Inactivated Poliomyelitis Vaccine, should be stored between 2° and 8°C (35° and 46°F). DO NOT FREEZE. Product which has been exposed to freezing should not be used.

Do not use after expiration date.

HOW SUPPLIED

Td Polio Adsorbed - Tetanus and Diphtheria Toxoids Adsorbed and Inactivated Poliomyelitis Vaccine is supplied in packages containing:

Ampoules	5 x 0.5 mL	(Single Dose)
Vial	1 x 5 mL	(Multi-dose)

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Product Information as of September 2001.

Manufactured by:
Aventis Pasteur Limited
Toronto, Ontario, Canada

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

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