QUADRACEL™

Component Pertussis Vaccine and Diphtheria and Tetanus Toxoids Adsorbed Combined with Inactivated Poliomyelitis Vaccine

For Active Immunization against Diphtheria, Tetanus, Whooping Cough and Poliomyelitis

DESCRIPTION

QUADRACEL™, Component Pertussis Vaccine and Diphtheria and Tetanus Toxoids Adsorbed Combined with Inactivated Poliomyelitis Vaccine, as supplied by Aventis Pasteur Limited, is a sterile, cloudy, uniform suspension of component pertussis vaccine, diphtheria and tetanus toxoids adsorbed on aluminum phosphate and suspended in water for injection and combined with inactivated poliomyelitis vaccine (Diploid Cell Origin - DCO). Component pertussis is an acellular pertussis vaccine composed of five purified pertussis antigens.

Each dose (0.5 mL) contains:	
pertussis toxoid (PT)	20 µg
filamentous haemagglutinin (FHA)	20 µg
fimbriae (agglutinogens 2 + 3)	5 µg
pertactin (69kDa membrane protein)	3 µg
diphtheria toxoid	15 Lf
tetanus toxoid	5 Lf
aluminum phosphate	1.5 mg
purified inactivated poliomyelitis vaccine:	Type 1 Mahoney
	Type 2 M.E.F.1
	Type 3 Saukett

0.6% ± 0.1% 2-phenoxyethanol added as preservative.

By calculation, the vaccine contains 10 ppm Tween 80 and less than 1 ppm of bovine serum. Trace amounts of polymyxin B and neomycin may be present from the cell growth medium.

CLINICAL PHARMACOLOGY

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

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 practised in Canada since 1930, resulting in a decline in morbidity and mortality. Fewer than 5 cases are now reported annually in Canada. The case-fatality rate remains 5 - 10%, with the highest death rates in the very young and elderly. 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]

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, provides long-lasting protection, and is recommended for the whole population. Only 2 to 3 cases of tetanus are now reported annually in Canada.[1] Tetanus toxoid is prepared by detoxification of tetanus toxin with formaldehyde.

Injection of bacterial proteins such as diphtheria and tetanus 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, circulating antibodies to tetanus and diphtheria toxoids gradually decline but are thought to persist at protective levels for up to 10 years.[1] Tetanus and diphtheria toxoid boosters are recommended every 10 years.

Pertussis (whooping cough) is a highly communicable bacterial disease caused by *Bordetella pertussis*. Severity and mortality are greatest in infancy, and even infants born to apparently immune mothers are highly susceptible to infection, particularly if maternal immunity was induced by whole-cell pertussis vaccine. During the last 40 years, vaccination with whole-cell pertussis vaccine has been widely practised in Canada and the incidence of pertussis decreased by over 90% although outbreaks of pertussis continue to occur. Hospitalizations for pertussis are still common in Canada and several deaths from pertussis occur each year, particularly in unimmunized infants.[3] Controversy regarding the safety of whole-cell pertussis vaccine during the 1970s led to several studies of the benefits and risks of this vaccination during the 1980s. These epidemiologic analyses clearly indicate that the benefits of the pertussis immunization program outweigh the risks.[4,5] Acellular pertussis vaccines consisting of purified fractions of the *Bordetella pertussis* bacterium have been used effectively to control pertussis in children 2 years of age or older in Japan since 1981.[6]

In a randomized, double-blind controlled clinical trial conducted in Sweden with 82,892 infants comparing 3 acellular pertussis and one European whole-cell DPT vaccines, 20,746 infants received the formulation of TRIPACEL™ contained in QUADRACEL™, Component Pertussis Vaccine and Diphtheria and Tetanus Toxoids Adsorbed Combined with Inactivated Poliomyelitis Vaccine and Haemophilus b Conjugate Vaccine (Tetanus Protein - Conjugate) at 2, 4 and 6 (2,552 infants) or 3, 5 and 12 (18,194 infants) months of age. TRIPACEL™ and the European whole-cell DPT vaccine had similar and high efficacy against culture-confirmed pertussis irrespective of duration. The other acellular pertussis combination vaccines were less effective.[7, 8] Rates of adverse events were less than or comparable to the rates in the other acellular pertussis and European whole-cell DPT groups in this study.[7, 8]

A randomized controlled efficacy study was conducted in Sweden using the formulation of TRIPACEL™, Component Pertussis Vaccine Combined with Diphtheria and Tetanus Toxoids Adsorbed, which contained lower concentrations of PT, FHA than the current formulation. In this study, 2,551 infants received TRIPACEL™ and 2,539 infants received a control vaccine containing diphtheria and tetanus toxoids at 2, 4 and 6 months of age. TRIPACEL™ demonstrated a clinical efficacy of 85.1% against pertussis disease (defined as 21 days of paroxysmal cough with culture or serologic confirmation of infection with *Bordetella pertussis*).[8,9]

Poliomyelitis is caused by infection with one of the 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 1978-79, 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[10], 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.[8]

In clinical trials conducted in Canada, more than 3,000 children have received QUADRACEL™, Component Pertussis Vaccine and Diphtheria and Tetanus Toxoids Adsorbed Combined with Inactivated Poliomyelitis Vaccine, alone or used to reconstitute Act-HIB®, Haemophilus b Conjugate Vaccine (Tetanus Protein - Conjugate). Whether given at 2, 4, 6 months, at 18 - 19 months (fourth dose) or at the 4 - 6 year booster, QUADRACEL™ produced comparable anti-tetanus, diphtheria and polio responses to the DPT Polio Adsorbed control. Anti-PRP responses were comparable as well. Although QUADRACEL™ contains 15 Lf of diphtheria toxoid versus the 25 Lf of diphtheria toxoid in DPT Polio Adsorbed, no significant differences in diphtheria antitoxin responses were seen in any of the age groups. Responses to pertussis antigens PT, FHA and pertactin were significantly higher in QUADRACEL™ recipients than in recipients of DPT Polio Adsorbed.

TABLE 1[8] COMPARISON OF QUADRACEL™ WITH WHOLE-CELL PERTUSSIS COMBINATIONS SEROLOGIC RESULTS

	GEOMETRIC MEAN TITRE (GMT)					
	7 months		19 - 20 months		4 - 6 years	
ANTIGEN	DPT Polio //PRP-T* (n = 105)	QUADRACEL™ (n = 108)	DPT Polio// PRP-T* (n = 94)	QUADRACEL™ (n = 92)	DPT Polio (n = 30)	QUADRACEL™ (n = 126)
Diphtheria	0.29	0.36	6.82	7.07	17.0	15.1
Tetanus	0.63	1.61	5.40	6.78	5.54	5.10
Agglutinins	438	444	642	848	1,315	1,939
PT	15.2	103	44.6	116	47.9	123.2
FHA	31.4	165	72.6	156	119.3	176.2
Pertactin	8.9	40.5	26.4	77	41.2	64.2
FIM	355	332	719	877	479	738
Polio 1	889	702	11,873	9,311	15,462	10,903
Polio 2	2,597	2,595	21,038	18,331	23,661	27,337
Polio 3	2,726	1,837	10,675	12,492	10,540	9,165

* Act-HIB® reconstituted with Aventis Pasteur Limited's DPT Polio Adsorbed.

With the exception of tetanus, no differences were found in immunogenicity when QUADRACEL™ was used to reconstitute Act-HIB® or the two vaccines were given at separate sites. Anti-PRP responses were comparable. All children were protected against polio. Pertussis responses were not affected by method of administration. Tetanus antitoxin levels were lower in the combined vaccine groups, but all children had protective levels (≥0.01 EU/mL). Following the 18-month dose, all children had tetanus antitoxin levels ≥0.10 EU/mL.

QUADRACEL™ was significantly less reactogenic than DPT Polio Adsorbed.

INDICATIONS

QUADRACEL™, Component Pertussis Vaccine and Diphtheria and Tetanus Toxoids Adsorbed Combined with Inactivated Poliomyelitis Vaccine, is indicated for the primary immunization of infants, at or above the age of two months and as a booster in children up to their 7th birthday against diphtheria, tetanus, whooping cough and poliomyelitis.

When both vaccines are indicated, QUADRACEL™ may be used to reconstitute Act-HIB®, Haemophilus b Conjugate Vaccine (Tetanus Protein - Conjugate) for simultaneous administration of all 5 antigens in a single injection. QUADRACEL™ must **not** be mixed in the same syringe with any other vaccines.

Because simultaneous administration of common childhood vaccines is not known to affect the efficacy or safety of any of the routine recommended childhood vaccines, if return of a vaccine recipient for further immunization is doubtful, simultaneous administration of all vaccines appropriate for age and previous vaccination status (including MMR, other *Haemophilus influenzae* type b conjugate vaccines, hepatitis B vaccine) at separate sites with separate syringes is indicated.[5]

Human Immunodeficiency Virus (HIV) Infected Persons
HIV-infected individuals, both asymptomatic and symptomatic, should be immunized against diphtheria, pertussis, tetanus and poliomyelitis according to standard schedules.[1]

Children who have had tetanus or diphtheria should still be immunized since these clinical infections do not always confer immunity.[1] Children who have had natural pertussis can continue to receive pertussis-containing vaccines.[3]

Infants born prematurely whose clinical condition is satisfactory should be vaccinated according to their chronological age from birth.[5]

CONTRAINDICATIONS

General

Immunization with QUADRACEL™, Component Pertussis Vaccine and Diphtheria and Tetanus Toxoids Adsorbed Combined with 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 QUADRACEL™ (see components listed in DESCRIPTION), or an allergic or anaphylactic reaction to a previous dose of DPT Polio Adsorbed are contraindications to vaccination.[1]

QUADRACEL™ should not be administered to children after their 7th birthday or to adults because of the quantity of diphtheria toxoid and because pertussis is less severe in these age groups than in infants and young children.

Relative Contraindications: (Based on experience with whole-cell pertussis vaccine)
Hypotonic-hyporesponsive episodes (HHE): No long term sequelae have been associated with HHE; however, because there are no data on administration of component pertussis vaccine to infants and children who have experienced HHE it may be prudent in areas of low pertussis incidence to withhold the pertussis component and continue immunization with DT Polio Adsorbed in children who have experienced a HHE following a previous dose of pertussis-containing vaccine. Children can continue immunization with QUADRACEL™ if the incidence of disease is high in their area.[1]

Deferral

Deferral of the pertussis component of QUADRACEL™ should be considered in children with a progressive, evolving, or unstable neurologic condition (including seizures) because administration of the pertussis component may coincide with the onset of overt manifestations of such disorders and result in confusion about causation. It is prudent to delay initiation of immunization with pertussis vaccine until further observation and study have clarified the child's neurologic status. In addition, the effect of treatment, if any, can be assessed. Immunization with QUADRACEL™ should be reinstituted when the condition has resolved, been corrected or controlled.[1]

When immunization with pertussis vaccine is contraindicated or deferred, immunization with diphtheria and tetanus toxoids and poliomyelitis vaccine, when necessary, may be continued using DT Polio Adsorbed.

Elective immunization of individuals over 6 months of age should be deferred during an outbreak of poliomyelitis because of the risk of provocation paralysis.[11,12,13]

WARNINGS

Intramuscular injections should be given with care in patients suffering from coagulation disorders because of the risk of hemorrhage.[1]

If QUADRACEL™, Component Pertussis Vaccine and Diphtheria and Tetanus Toxoids Adsorbed Combined with Inactivated Poliomyelitis Vaccine, is used in persons with malignancies, receiving immunosuppressive therapies, including irradiation, antimetabolites, alkylating agents, cytotoxic drugs, or who are otherwise immunocompromised (including HIV-infected individuals), 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 per day of prednisone orally for more than 2 weeks, should be considered to have a compromised immune system.[1]

As with any vaccine, immunization with QUADRACEL™ may not protect 100% of susceptible individuals.

The use of fractional doses in an attempt to reduce the severity of adverse reactions cannot be recommended because there is insufficient evidence on the safety or efficacy of such smaller doses.[1]

PRECAUTIONS

General

The possibility of allergic reactions in individuals 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.[5,14]

Before administration of any vaccine, 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 a current knowledge of the literature concerning the use of the vaccine under consideration.

Antipyretic Prophylaxis: Administration of acetaminophen (15 mg/kg per dose) or other appropriate antipyretic at the time of immunization and at 4 and 8 hours after immunization decreases the incidence of febrile and local reactions.[1] Since convulsions after whole-cell pertussis vaccine are almost always associated with fever, antipyretic prophylaxis may benefit children at increased risk of seizures. For such children, administration of an antipyretic every 4 to 6 hours for as long as 24 hours after vaccination should be considered. Caregivers should be aware that antipyretic therapy could also obscure fever caused by concomitant, unrelated infection.[5]

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

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.[15]

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

A family history of convulsions in parents and siblings is not a contraindication to pertussis vaccination and children with such family histories should receive pertussis-containing vaccines according to the recommended schedule.[4] Parents of infants and children with family histories of convulsions should be informed of their children's increased risk of seizures following administration of any vaccine causing a febrile reaction.[16] Acetaminophen prophylaxis is particularly recommended for children with a personal or family history of convulsions.[1]

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.

Before administration of QUADRACEL™, health-care personnel should inform the 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 before immunization.

ADVERSE REACTIONS

In clinical trials done in Canada, QUADRACEL™, Component Pertussis Vaccine and Diphtheria and Tetanus Toxoids Adsorbed Combined with Inactivated Poliomyelitis Vaccine, had consistently lower rates of local and systemic reactions than DPT Polio Adsorbed, whether combined with Act-HIB® or given at separate sites. There was a trend towards increasing local reaction rates at the fourth and fifth doses, but these were still significantly lower than with whole-cell pertussis combination vaccines.[9]

TABLE 2[8] LOCAL ADVERSE REACTIONS (%) WITHIN 24 HOURS OF VACCINATION WITH QUADRACEL™

REACTION	2 Months (n = 111)	4 Months* (n = 109)	6 Months* (n = 109)	18-19 Months (n = 92)	**4-6 Years*** (n = 163)
Redness	1	7	12	15	19
Swelling	5	4	7	8	19
Tenderness	19	17	10	22	75

* Received QUADRACEL™ for previous dose(s).

** Received whole-cell pertussis combination vaccine for first 3 doses.

*** Received whole-cell pertussis combination vaccine for first 4 doses.

TABLE 3[8] SYSTEMIC ADVERSE REACTIONS (%) WITHIN 24 HOURS OF VACCINATION WITH QUADRACEL™

REACTION	2 Months (n = 111)	4 Months* (n = 109)	6 Months* (n = 109)	18-19 Months (n = 92)	** 4-6 Years*** (n = 163)
Fever	21	20	17	19	17
Fussiness	45	42	35	33	20
Crying	30	28	24	4	-
Decreased Activity	51	29	22	14	23
Decreased Eating	34	21	17	15	23
Vomiting	8	3	6	3	5
Diarrhea	8	8	10	8	2

* Received QUADRACEL™ for previous dose(s).

** Received whole-cell pertussis combination vaccine for first 3 doses.

*** Received whole-cell pertussis combination vaccine for first 4 doses.

In a clinical trial conducted in Sweden comparing 3 acellular pertussis vaccines and 1 whole-cell DPT vaccine, 20,745 infants received TRIPACEL™ at 2, 4 and 6 or 2, 5 and 12 months of age. Rates of adverse events were less than or comparable to the rates in the other acellular pertussis vaccine and whole-cell DPT groups in this study. The rates of reports of fever >40.5°C and seizures or suspected seizures were significantly higher following whole-cell DPT than following acellular pertussis vaccines.[7,8] Rates of hypotonic-hyporesponsive episodes were comparable, with 29 reports following administration of TRIPACEL™. No deaths or cases of encephalitis/acute encephalopathy, invasive bacterial infection, infantile spasms or anaphylactic reactions were reported within 48 hours of vaccination.[7,17,18]

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 pertussis antigens.[4] Death following vaccine-caused anaphylaxis has been reported.[19]

Localized reactions consisting of discomfort, pain, swelling and redness at the injection site may be associated with tetanus and diphtheria toxoids.[20,21] 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.

Systemic reactions, such as generalized urticaria, are uncommon. Influenza-like symptoms have been reported and usually occur within 12 hours of vaccination with diphtheria and tetanus toxoids.[21]

Neurological complications such as peripheral neuropathies[22,23] and demyelinating diseases of the central nervous system (CNS)[19] following some tetanus toxoids or diphtheria toxoids have been documented but are rare.[24] The U.S. 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).[19]

The following neurologic illnesses have been reported as temporally associated with some vaccines containing tetanus toxoid: neurological complications[25] including cochlear lesion,[26] brachial plexus neuropathies,[24,26] paralysis of the radial nerve,[22] paralysis of the recurrent nerve,[26] accommodation paresis, and EEG disturbances with encephalopathy (with or without permanent intellectual and/or motor function impairment).[27] In the differential diagnosis of polyradiculoneuropathies following administration of a vaccine containing tetanus toxoid, tetanus toxoid should be considered as a possible etiology.[19,28] The Institute of Medicine concluded that the evidence favours acceptance of a causal relation between tetanus toxoid and brachial neuritis.[19]

On the basis of a 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 DPT in children.[24]

Persistent nodules at the site of injection have occurred following the use of an adsorbed product, but this complication is unusual,[29] and may be related to subcutaneous administration. Sterile abscess at the site of injection has been reported following use of adsorbed vaccines (6 - 10 per million doses).[5]

QUADRACEL™ does not contain a whole-cell pertussis vaccine, however, persistent, inconsolable crying lasting 3 or more hours (1%) and high-pitched, unusual screaming (0.1%) have been reported after whole-cell DPT vaccination. The incidence of both of these events is significantly lower with QUADRACEL™.[9] Convulsions and a hypotonic-hyporesponsive state have each been reported to occur at a frequency of about 1:1,750 doses of whole-cell DPT.[1,5,27] Most convulsions are brief, generalized and self-limited, and are usually associated with fever. Neither febrile nor afebrile convulsions have been shown to be associated with subsequent seizure disorder.[5] Complete recovery, without persistent sequelae, has been observed on follow-up of children with hypotonic-hyporesponsive episodes or convulsions.[1,3,5] (See CONTRAINDICATIONS and PRECAUTIONS.)

Although there has been a concern about the possible association of severe neurologic illness (including encephalopathy [with or without permanent intellectual and/or motor function impairment]) occurring within 72 hours of the administration of whole-cell pertussis-containing vaccines to previously healthy infants, the risk of an association is so small compared to the background rate for these types of events that the question of causation probably cannot be answered.[1,3]

Reanalysis of the National Childhood Encephalopathy Study (NCES) in the United Kingdom has failed to confirm that there was an increased risk of permanent brain damage following acute neurological illness occurring within 7 days of whole-cell pertussis vaccination. Additional studies have also failed to demonstrate an association between pertussis vaccine and permanent neurologic sequelae[1] (including permanent intellectual and/or motor function impairment).

Sudden infant death syndrome (SIDS) has been reported in temporal relationship to the administration of vaccines containing diphtheria and tetanus toxoids and pertussis vaccine (DPT). Review of the evidence does not indicate a causal relationship between whole-cell DPT vaccine and SIDS. Studies showing a temporal relation between these events are consistent with the expected occurrence of SIDS over the age range in which DPT immunization usually occurs.[29,30]

As with any vaccine, there is the possibility that broad use of the vaccine could reveal rare adverse reactions not observed in clinical trials.

Physicians, nurses, and pharmacists should report any adverse occurrences temporally related to the administration of the product in accordance with local requirements and report to the Medical Director at Aventis Pasteur Limited, 1755 Steeles Avenue West, Toronto, Ontario, Canada, M2R 3T4.

DOSAGE

For primary immunization of infants the following routine QUADRACEL™, Component Pertussis Vaccine and Diphtheria and Tetanus Toxoids Adsorbed Combined with Inactivated Poliomyelitis Vaccine, immunization schedule is recommended: one 0.5 mL dose administered at 2, 4, 6 and 18 months of age.

If for any reason this schedule is delayed, it is recommended that three doses of 0.5 mL be administered with an interval of two months between doses, followed by a fourth dose of 0.5 mL administered approximately 6 - 12 months following the third dose.

A booster dose of 0.5 mL should be administered between four and six years of age (i.e., at the time of school entry). This booster dose is unnecessary if the fourth primary immunizing dose has been administered after the fourth birthday.[1]

Whenever feasible, QUADRACEL™ should be used for all doses in the vaccination series as there are no clinical data to support the use of QUADRACEL™ with any other licensed acellular pertussis combination vaccine in a mixed sequence. For situations where a different brand of DTaP or DTaP-IPV vaccine was originally used, or where the brand is unknown, please refer to the latest edition of Health Canada's *Canadian Immunization Guide*.

Thereafter, routine booster immunizations should be with Td or Td Polio, at intervals of 10 years. PERSONS 7 YEARS OF AGE AND OLDER SHOULD NOT BE IMMUNIZED WITH QUADRACEL™.[1]

ADMINISTRATION

Parenteral biological products should be inspected visually for extraneous particulate matter and/or discolouration 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 stoppered vial, do not remove either the 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 or into the anterolateral aspect of the mid-thigh (vastus lateralis muscle). In children >1 year of age, the deltoid is the preferred site since use of the anterolateral thigh results in frequent complaints of limping due to muscle pain.[1,31]

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, manufacturer and lot number.

STORAGE

QUADRACEL™, Component Pertussis Vaccine and Diphtheria and Tetanus Toxoids Adsorbed Combined with Inactivated Poliomyelitis Vaccine, should be stored at 2° to 8°C (35° to 46°F). DO NOT FREEZE. Product which has been exposed to freezing should not be used. Do not use vaccine after expiration date.

HOW SUPPLIED

Ampoule 5 x 0.5 mL (Single Dose)

QUADRACEL™ is also supplied in packages containing five single-dose vials of Act-HIB® and five 0.5 mL (single-dose) ampoules of QUADRACEL™ to be used for reconstitution in place of the diluent and sold under the name of PENTACEL™.

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