PEDIACEL®

Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed Combined with Inactivated Poliomyelitis Vaccine and Haemophilus b Conjugate Vaccine (Tetanus Protein – Conjugate)

Intramuscular injection. Suspension for injection.

DESCRIPTION

PEDIACEL®[Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed Combined with Inactivated Poliomyelitis Vaccine and Haemophilus b Conjugate Vaccine (Tetanus Protein – Conjugate)] is a sterile, uniform, cloudy, white to off-white suspension of diphtheria and tetanus toxoids and acellular pertussis vaccine adsorbed separately on aluminum phosphate combined with inactivated poliomyelitis vaccine (vero cell origin) types 1, 2 and 3 (IPV), and H. influenzae type b capsular polysaccharide (polyribosylribitol phosphate, PRP) covalently bound to tetanus protein, and suspended in water for injection. The acellular pertussis vaccine is composed of 5 purified pertussis antigens (PT, FHA, PRN and FIM).

INDICATIONS AND CLINICAL USE

PEDIACEL® is indicated for primary immunization of infants from the age of 2 months and in children up to 6 years of age (prior to their 7th birthday) against diphtheria, tetanus, pertussis (whooping cough), poliomyelitis and invasive H. influenzae type b disease. (See DOSAGE AND ADMINISTRATION.)

In infants, three infectons are to be given intramuscularly at 2, 4 and 6 months of age followed by a booster at 18 months of age.

Currently, Haemophilus b conjugate vaccines are not recommended for infants younger than 2 months of age.

Children who have had pertussis, tetanus, diphtheria or H. influenzae type b (Hib) invasive disease should still be immunized since these clinical infections do not always confer immunity. Children who have had natural pertussis can continue to receive pertussis – containing vaccines.

Human Immunodeficiency Virus (HIV)-infected persons, both asymptomatic and symptomatic, should be immunized against diphtheria, tetanus, pertussis, poliomyelitis and H. influenzae type b, according to standard schedules.

PEDIACEL® is not to be used for the treatment of diseases caused by Corynebacterium diphtheriae, Clostridium tetani, Bordetella pertussis, poliovirus or Haemophilus influenzae type b infections.

Pediatrics

PEDIACEL® is not indicated for persons less than 2 months or to persons 7 years of age or older.

Geriatrics

PEDIACEL® is not indicated for use in adult and elderly populations.

CONTRAINDICATIONS

Hypersensitivity

Known systemic hypersensitivity reaction to any component of PEDIACEL® or a life-threatening reaction after previous administration of the vaccine or a vaccine containing one or more of the same components are contraindications to vaccination. Because of uncertainty as to which component of the vaccine may be responsible, none of the components should be administered. Alternatively, such persons may be referred to an allergist for evaluation if further immunizations are considered.

Acute Neurological Disorders

The following events are contraindications to administration of any pertussis-containing vaccine, including PEDIACEL®:

Encephalopathy (e.g., coma, decreased level of consciousness, prolonged seizures) within 7 days of a previous dose of a pertussis-containing vaccine that is not attributable to another identifiable cause.

Progressive neurologic disorder, including infantile spasms, uncontrolled epilepsy, progressive encephalopathy. Pertussis vaccine should not be administered to persons with such conditions until a treatment regimen has been established and the condition has stabilized.

WARNINGS AND PRECAUTIONS

General

Before administration of PEDIACEL®, health-care providers should inform the parent or guardian of the recipient to be immunized of the benefits and risks of immunization, inquire about the recent health status of the recipient, review the recipient's history concerning possible hypersensitivity to the vaccine or similar vaccine, previous immunization history, the presence of any contraindications to immunization and comply with any local requirements with respect to information to be provided to the parent or guardian before immunization and the importance of completing the immunization series.

It is extremely important that the 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)

The rates and severity of adverse events in recipients of tetanus toxoid are influenced by the number of prior doses and level of pre-existing antitoxins.

As with any vaccine, PEDIACEL® may not protect 100% of vaccinated individuals.

Vaccines that contain Hib antigen do not provide protection against infections with other types of H. influenzae, or against meningitis of other origin.

Under no circumstances can the tetanus protein contained in conjugate vaccines containing tetanus toxoid as protein carrier be used to replace the usual tetanus vaccination.

Sudden infant death syndrome (SIDS) has occurred in infants following administration of DTaP vaccines. By chance alone, some cases of SIDS can be expected to follow receipt of PEDIACEL®.

Administration Route Related Precautions: Do not administer PEDIACEL® by intravascular injection; ensure that the needle does not penetrate a blood vessel.

Intradermal or subcutaneous routes of administration are not to be utilized.

PEDIACEL® should not be administered into the buttocks.

Granuloma or sterile abscess at the injection site has been reported with a product containing the same antigens.

Febrile or Acute Disease: Vaccination should be postponed in cases of acute or febrile disease. However, a disease with low-grade fever should not usually be a reason to postpone vaccination.

If any of the following events occur within the specified period after administration of a whole-cell pertussis vaccine or a vaccine containing an acellular pertussis component, the decision to administer PEDIACEL® should be based on careful consideration of potential benefits and possible risks.

- Temperature of ≥40.5°C (105°F) within 48 hours, not attributable to another identifiable cause;
- Collapse or shock-like state (hypotonic-hyporesponsive episode) within 48 hours;
- Persistent crying lasting ≥3 hours within 48 hours;
- Convulsions with or without fever within 3 days.

Hematologic

Because any intramuscular injection can cause an injection site hematoma in persons with any bleeding disorders, such as hemophilia or thrombocytopenia, or in persons on anticoagulant therapy, intramuscular injections with PEDIACEL® should not be administered to such persons unless the potential benefits outweigh the risk of administration. If the decision is made to administer any product by intramuscular injection to such persons, it should be given with caution, with steps taken to avoid the risk of hematoma formation following injection.

Immune

The possibility of allergic reactions in persons sensitive to components of the vaccine should be evaluated. Hypersensitivity reactions may occur following the use of PEDIACEL® even in persons with no prior history of hypersensitivity to the product components. Cases of allergic or anaphylactic reaction have been reported after receiving some preparations containing diphtheria and tetanus toxoids and/or pertussis antigens.

As with all other products, 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. Health-care providers should be familiar with current recommendations for the initial management of anaphylaxis in non-hospital settings, including proper airway management.

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. Nevertheless, vaccination of persons with chronic immunodeficiency such as HIV infection is recommended even if the antibody response might be limited.

Neurologic

A review by the US Institute of Medicine (IOM) found evidence for a causal relation between tetanus toxoid and both brachial neuritis and Guillain-Barré syndrome (GBS). If GBS occurred within 6 weeks of receipt of prior vaccine containing tetanus toxoid, the decision to give PEDIACEL® or any vaccine containing tetanus toxoid should be based on careful consideration of potential benefits and possible risks.

A few cases of demyelinating diseases of the central nervous system, peripheral mononeuropathies, and cranial mononeuropathies have been reported following vaccines containing tetanus and/or diphtheria toxoids, although the IOM concluded that the evidence is inadequate to accept or reject a causal relation between these conditions and vaccination.

For infants or children at higher risk for seizures than the general population, an appropriate antipyretic may be administered (in the dosage recommended in its prescribing information) at the time of vaccination with a vaccine containing an acellular pertussis component (including PEDIACEL®) and for the following 24 hours, to reduce the possibility of post-vaccination fever.

Hypotonic-hyporesponsive episodes (HHEs) rarely follow vaccination with whole-cell pertussis containing DTP vaccines and occur even less commonly after acellular pertussis-containing DTP vaccines and DT vaccines. A history of HHEs is not a contraindication to the use of acellular pertussis vaccines but recommends caution in these cases.

Pregnant Women

The vaccine should not be administered to pregnant women.

Nursing Women

The vaccine should not be administered to nursing women.

Pediatric

The potential risk of apnea and the need for respiratory monitoring for 48 - 72 hours should be considered when administering the primary immunization series to very premature infants (born ≤28 weeks of gestation) and particularly for those with a previous history of respiratory immaturity. As the benefit of vaccination is high in this group of infants, vaccination should not be withheld or delayed.

ADVERSE REACTIONS

Clinical Trial Adverse Reactions

Because clinical trials are conducted under widely varying conditions, adverse reaction rates

observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect rates observed in practice. The adverse reaction information from clinical trials does, however, provide a basis for identifying the adverse events that appear to be related to vaccine use and for approximating rates of those events.
In a randomized, controlled clinical trial conducted in Canada, 339 infants were immunized with PEDIACEL® at 2, 4 and 6 months of age. In addition, 301 of these children were immunized as toddlers at 18 months. Injection site reactions were generally mild. Up to one third of children receiving PEDIACEL® experienced some degree of redness, swelling or tenderness around the injection site. The frequency of solicited injection site and systemic reactions observed in a clinical trial within 24 hours of any dose of PEDIACEL® given at 2, 4, 6 and 18 months of age are presented below.
Very Common: ≥10%
Common: ≥1% and <10%
Gastrointestinal Disorders
Common: Diarrhea, vomiting.
General Disorders and Administration Site Conditions
Very Common: Injection site tenderness, swelling, redness, fever (≥38.0°C), crying, eating less, fussiness, less active.
Data from Post-Marketing Experience
The following additional adverse events have been spontaneously reported during the post-marketing use of PEDIACEL® worldwide. Because these events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.
Immune System Disorders
Hypersensitivity, anaphylactic reaction (such as urticaria, angioedema).
Psychiatric Disorders
Irritability , screaming.
Nervous System Disorders
Convulsion (with or without fever), prolonged or unusual high-pitched crying, hypotonic hyporesponsive episode (infant appears pale, hypotonic [limp] and unresponsive to parents). To date, this condition has not been associated with any permanent sequelae Somnolence
Vascular Disorders
Pallor
Respiratory, Thoracic and Mediastinal Disorders
Apnea
Skin and Subcutaneous Tissue Disorders
Erythema, rash.
Musculoskeletal, Connective Tissue and Bone Disorders
Pain in vaccinated limb.
General Disorders and Administration Site Conditions
High fever (>40.5°C), injection site mass, , asthenia, and listlessness.
Large injection site reactions (>50 mm) including extensive limb swelling which may extend from the injection site beyond one or both joints, have been reported in children following PEDIACEL® administration. These reactions usually start within 24 - 72 hours after vaccination, may be associated with erythema, warmth, tenderness or pain at the injection site and resolve spontaneously within 3 to 5 days. The risk appears to be dependent on the number of prior doses of acellular pertussis containing vaccine, with a greater risk following the 4th and 5th doses.
Edematous reactions affecting one or both lower limbs have occurred following vaccination with H. influenza type b containing vaccines. When this reaction occurs, it does so mainly after primary injections and is observed within the first few hours following vaccination. Associated symptoms may include cyanosis, redness, transient purpura and severe crying. All events resolved spontaneously without sequelae within 24 hours.

DRUG INTERACTIONS
Vaccine-Drug Interactions
Immunosuppressive treatments may interfere with the development of the expected immune response. (See WARNINGS AND PRECAUTIONS.)
Concomitant Vaccine Administration
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. Vaccines administered simultaneously should be given using separate syringes at separate sites. Simultaneous administration is suggested, particularly when there is concern that a person may not return for subsequent vaccination.
PEDIACEL® should not be mixed in the same syringe with other parenterals.
Vaccine-Laboratory Test Interactions
Antigenuria has been detected in some instances following administration of a vaccine containing Hib antigen. Therefore, urine antigen detection may not have definite diagnostic value in suspected H. influenzae type b disease within two weeks of immunization.

DOSAGE AND ADMINISTRATION
Recommended Dose
1 dose = 0.5 mL
The immunization schedule with PEDIACEL® should follow local recommendations. As a guide, PEDIACEL® may be administered as a 4-dose series starting as early as 2 months of age with 3 doses at an interval of 2 months between each dose, followed by a booster dose approximately 6 to 12 months after the third dose.
Whenever feasible, PEDIACEL® should be used for all 4 doses in the vaccination series as there are no clinical data to support the use of PEDIACEL® with any other licensed acellular pertussis combination vaccine in a mixed sequence.
Premature infants whose clinical condition is satisfactory should be immunized with full doses of vaccine at the same chronological age and according to the same schedule as full-term infants, regardless of birth weight.
Fractional doses (doses <0.5 mL) should not be given. The effect of fractional doses on the safety and efficacy has not been determined.
PEDIACEL® should not be administered to persons less than 2 months or to persons 7 years of age or older. (See INDICATIONS AND CLINICAL USE.)
Administration
Inspect for extraneous particulate matter and/or discolouration before use. If these conditions exist, the product should not be administered.
Shake the vial well until a uniform, cloudy, suspension results. Cleanse the vial stopper with a suitable germicide prior to withdrawing the dose. Do not remove either the stopper or the metal seal holding it in place.
Aseptic technique must be used. Use a separate, sterile syringe and needle, or a sterile disposable unit, for each individual patient to prevent disease transmission. Needles should not be recapped but should be disposed of according to biohazard waste guidelines.
Before injection, the skin over the site to be injected should be cleansed with a suitable germicide. Administer the total volume of 0.5 mL intramuscularly (I.M.). In infants younger than 1 year, the anterolateral aspect of the thigh provides the largest muscle and is the preferred site of injection. In older children, the deltoid muscle is usually large enough for injection.

STORAGE AND STABILITY
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.

DOSAGE FORMS, COMPOSITION AND PACKAGING
Dosage Forms
PEDIACEL® is supplied as a sterile, uniform, cloudy, white to off-white suspension in a vial.
Composition
Each single dose (0.5 mL) contains:

Active Ingredients	
Diphtheria Toxoid (D) adsorbed	15 Lf (≥ 30 UI)
Tetanus Toxoid (T) adsorbed	5 Lf (≥ 40 UI)
Acellular Pertussis	
Pertussis Toxoid adsorbed(PT)	20 µg
Filamentous Haemagglutinin adsorbed (FHA)	20 µg
Pertactin (PRN) adsorbed	3 µg
Fimbriae Types 2 and 3 (FIM) adsorbed	5 µg
Inactivated Poliomyelitis Vaccine	
Type 1 (Mahoney)	40 D-antigen units
Type 2 (MEF1)	8 D-antigen units
Type 3 (Saukett)	32 D-antigen units
Purified Capsular	
Polysaccharide (PRP) of Haemophilus influenzae	
Type b covalently bound to 20 µg of Tetanus Protein	10 µg
Other Ingredients	
Excipients	
Aluminum Phosphate (adjuvant)	1.5 mg (0.33+- 0.03 mg)
2-phenoxyethanol	0.6% v/v (3.33 mg)
Polysorbate 80	≤0.1% w/v (by calculation

Manufacturing Process Residuals
Bovine serum albumin, neomycin, polymyxin B, streptomycin and formaldehyde are present in trace amounts.
Packaging
PEDIACEL® is supplied in 0.5 mL single dose glass vials.
The vials are made of Type 1 glass.
The container closure system for PEDIACEL® is free of latex (natural rubber).
PEDIACEL® is available in a package of:
1 single dose vial
5 single dose vials

Manufactured by:
Sanofi Pasteur Limited
Toronto, Ontario, Canada

License Holder:
Medici Ltd.
8 Tzoran St. Netanya ,Israel

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