NAME OF THE MEDICINAL PRODUCT

POLIACEL®

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

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each single dose (approximately 0.5 mL) after reconstitution contains:

Purified Polyribosylribitol Phosphate Capsular Polysaccharide (PRP) of *Haemophilus influenzae* type b covalently bound to 20 µg of Tetanus Protein	10 µg
Diphtheria toxoid	15 Lf
Tetanus toxoid	5 Lf
Pertussis antigens:	
Pertussis toxoid (PT)	20 µg
Filamentous haemagglutinin (FHA)	20 µg
Pertactin (PRN)	3 ug
Fimbriae Types 2 and 3 (FIM)	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

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

After reconstitution, POLIACEL® is a sterile uniform, cloudy, white to off-white suspension for injection.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Primary vaccination of infants, at or above the age of two months and as a booster in children up to their 6th birthday against diphtheria, tetanus, pertussis, poliomyelitis and invasive *Haemophilus influenzae* type b infection.

4.2 Posology and method of administration

1 dose = about 0.5 mL.

Always to be administered in accordance with the prescription of the doctor.

For routine immunization, POLIACEL® is recommended as a 4-dose series, with a single dose of POLIACEL® at 2, 4, 6 and 12 months of age.

If for any reason this schedule is delayed, it is recommended that 3 doses be administered with an interval of 2 months between each dose, followed by a fourth dose administered approximately 6 to 12 months after the third dose.

Whenever feasible, POLIACEL® should be used for all 4 doses in the vaccination series as there are no clinical data to support the use of POLIACEL® 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.

Administer the vaccine intramuscularly. In infants <1 year of age, the preferred site is 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.

Do not inject by the intravascular route: ensure that the needle does not penetrate a blood vessel. Intradermal or subcutaneous routes of administration are not to be utilized.

POLIACEL® should not be administered into the buttocks.

4.3 Contraindications

Hypersensitivity

Allergy to any component of this vaccine (see components listed in Composition) or an allergic or anaphylactic reaction to a previous dose of this 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 POLIACEL®:

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.

4.4 Special warnings and precautions for use

General

Before administration of POLIACEL®, health-care providers should inform the parent or guardian of the recipient 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 signs or symptoms of an adverse reaction after a previous dose of vaccine. (See 4.3 Contraindications and 4.8 Undesirable Effects .)

As with any vaccine, POLIACEL® may not protect 100% of susceptible individuals.

Vaccines that contain Hib antigen do not provide protection against infections with other types of *Haemophilus 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.

Edematous reaction affecting one or both lower limbs has occurred following vaccination with *Haemophilus influenzae* 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. In reported cases, all events resolved spontaneously without sequelae within 24 hours.

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 administration of DTaP, IPV or Hib vaccines.

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

The Advisory Committee on Immunization Practices (ACIP) recommends that 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 POLIACEL® should be based on careful consideration of potential benefits and possible risks.

- Temperature of ≥40.5°C 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 POLIACEL® 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 POLIACEL® 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.

Although anaphylaxis is rare, facilities for its management must always be available during vaccination. Epinephrine Hydrochloride solution (1:1,000), airway management, and other appropriate agents should be available for immediate use in case an anaphylactic or acute hypersensitivity reaction occurs.

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

Neurologic

If Guillain-Barré syndrome (GBS) occurred within 6 weeks of receipt of prior vaccine containing tetanus toxoid, the decision to give POLIACEL® or any vaccine containing tetanus toxoid should be based on careful consideration of potential benefits and possible risks

It is recommended that 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 POLIACEL®) and for the following 24 hours, to reduce the possibility of post-vaccination fever.

A history of hypotonic-hyporesponsive episodes is not a contraindication to the use of acellular pertussis vaccines but caution is recommended in these cases.

4.5 Interaction with other medicinal products and other forms of interaction

Immunosuppressive treatments may interfere with the development of the expected immune response.

Concomitant Vaccine Administration

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, hepatitis B vaccine) at separate sites with separate syringes is indicated.

POLIACEL® 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 *Haemophilus influenzae* type b disease within two weeks of immunization.

4.6 Pregnancy and lactation

The vaccine should not be administered during pregnancy and lactation.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

Clinical Trial Adverse Drug Reactions

Table 1 below provides a summary of the frequency of solicited reactions observed within 24 hours following each dose of POLIACEL®. Injection site reactions were generally mild. Up to approximately one third of children receiving POLIACEL® experienced some degree of redness, swelling or tenderness around the injection site. The frequency and duration of severe redness and swelling was higher after the fourth dose in toddlers than in the previous three doses in infants, however severe tenderness did not increase with the fourth dose. Severe systemic reactions were infrequent with POLIACEL® and experienced by less than 2% of children. No infant immunized with POLIACEL® and only one toddler immunized with POLIACEL® experienced a fever >40°C.

Table 1: Frequency (%) of Solicited Reactions Observed 24 Hours Following a Single Dose of POLIACEL® Administered at 2, 4, 6 and 18 Months of Age

Solicited Reactions	2 months (N = 333)	4 months (N = 327)	6 months (N = 320)	18 months (N = 295)
Injection Site Reactions				
Redness	8.7	11.9	11.6	19.3
Swelling	11.7	8.8	9.4	14.2
Tenderness	26.4	27.1	19.7	28.1
Systemic Reactions				
Fever ≥38.0°C	18.6	19.5	15.0	21.5
Less Active	46.8	30.8	20.7	9.8
Fussiness	43.5	53.4	37.0	30.2
Crying	30.6	41.5	27.6	18.6
Eating Less	27.6	20.7	15.4	16.9
Diarrhea	10.2	7.6	6.6	5.4
Vomiting	8.7	5.2	4.7	4.4

Data from Post-Marketing Experience

The following additional adverse events have been spontaneously reported between 1997 and 2006, during the post-marketing use of POLIACEL® worldwide. Because these events are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure. Decisions to include these events in labelling were based on one or more of the following factors: 1) severity of the event, 2) frequency of reporting, or 3) strength of causal connection to POLIACEL®.

Immune system disorders

Hypersensitivity (allergic reactions, such as rash and urticaria).

Psychiatric disorders

Screaming

Nervous system disorders

Convulsion, somnolence, HHE, hypotonia.

Cardiac disorders

Cyanosis

Vascular disorders

Pallor

General disorders and administration site conditions

Injection site reactions (including inflammation, mass, abscess and sterile abscess), edema.

Very rarely, large injection site reactions (>50 mm), including limb swelling which may extend from the injection site beyond one or both joints have been reported in children following POLIACEL® 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 3-5 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.

4.9 Overdose
Not applicable.

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Pharmacotherapeutic Group: Vaccine against diphtheria, tetanus, pertussis, poliomyelitis and hemophilus influenza
ATC Code: J07CA

5.2 Pharmacokinetic properties
As for all vaccines, pharmacokinetic data being non-relevant.

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Excipients: Aluminum phosphate (adjuvant), 2-phenoxyethanol, Polysorbate 80, Tris (hydroxymethyl aminomethane), sucrose.
Manufacturing process residuals: Bovine serum albumin, formaldehyde, glutaraldehyde, neomycin, polymyxin B,

6.2 Incompatibilities
In the absence of compatibility studies, POLIACEL must not be mixed with any vaccine or other medicinal products.

6.3 Shelf life
36 months.

6.4 Special precautions for storage
Store in a refrigerator (at 2°C to 8°C).
Do not freeze. Discard the vaccine if it has been frozen.
The vaccine should be used immediately after reconstitution.
Do not use vaccine after expiration date.

6.5 Presentations: The stoppers of the vials do not contain latex (natural rubber).
5 dose package containing QUADRACEL® (5 x 0.5 mL vials) for reconstitution of Act-HIB® (5 x 1 dose vials).

6.6 Special precautions for disposal and other handling
Instructions for use

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

Reconstitution of Freeze-Dried Product and Withdrawal from Stoppered Vial

Reconstitute Haemophilus b Conjugate Vaccine (Tetanus Protein Conjugate) with the Component Pertussis Vaccine and Diphtheria and Tetanus Toxoids Adsorbed Combined with Inactivated Poliomyelitis Vaccine. Cleanse the Component Pertussis Vaccine and Diphtheria and Tetanus Toxoids Adsorbed Combined with Inactivated Poliomyelitis and Haemophilus b Conjugate Vaccine (Tetanus Protein Conjugate) vial stoppers with a suitable germicide before reconstitution. Do not remove from either vial the stoppers or the metal seals holding them in place. Thoroughly but gently shake the vial of Component Pertussis Vaccine and Diphtheria and Tetanus Toxoids Adsorbed Combined with Inactivated Poliomyelitis Vaccine, withdraw the entire contents of the liquid vaccine and inject slowly into the vial of lyophilized Haemophilus b Conjugate Vaccine (Tetanus Protein Conjugate). Shake the vial now containing POLIACEL® thoroughly until a uniform, cloudy, white to off-white suspension results. Withdraw the total volume of reconstituted combined vaccine. POLIACEL® should be used immediately after reconstitution.

Disposal

Any unused product or waste material should be disposed of in accordance with local requirements. Needles should not be reprocessed.

7. LICENSE HOLDER

Medici Medical Ltd.,
2 Hapnina St., Ra'anana 43000.

8. MANUFACTURER

Sanofi Pasteur Limited
Toronto, Ontario, Canada

The format of this leaflet was determined by the Ministry of Health and its content was checked and approved on July 2010.