Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Pediacel Suspension for Injection in Pre-filled Syringe
Diphtheria, Tetanus, Pertussis (acellular component), poliomyelitis (inactivated) and Haemophilus type b conjugate vaccine (adsorbed)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 0.5 mL dose contains:

Diphtheria Toxoid	not less than 30 IU
Tetanus Toxoid	not less than 40 IU
Acellular Pertussis Antigens	
- Pertussis Toxoid (PT)	20 micrograms
- Filamentous Haemagglutinin (FHA)	20 micrograms
- Pertactin (PRN)	3 micrograms
- Fimbriae Types 2 and 3 (FIM)	5 micrograms
Poliovirus (Inactivated)*	
- Type 1 (Mahoney)	40 D antigen units†
- Type 2 (MEF-1)	8 D antigen units†
- Type 3 (Saukett)	32 D antigen units†
Haemophilus influenzae Type b Polysaccharide	
- (Polyribosylribitol Phosphate)	10 micrograms
- Conjugated to Tetanus Toxoid (PRP-T)	20 micrograms
Adsorbed on aluminium phosphate (0.33 mg aluminium)	1.5 mg

* Produced in Vero cells.

† or equivalent antigenic quantity determined by a suitable immunochemical method.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Suspension for Injection in pre-filled syringe
Cloudy, white to off-white suspension

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

PEDIACEL is indicated for primary and booster vaccination against diphtheria, tetanus, pertussis, poliomyelitis and invasive *Haemophilus influenzae* type b disease in infants and children from the age of 6 weeks up to the fourth birthday. PEDIACEL should be used in accordance with applicable official recommendations.

4.2 Posology and method of administration

Posology

Paediatric population

Primary Vaccination

The primary vaccination series consists of 2 or 3 doses of 0.5 mL and may be commenced from 6 weeks of age according to applicable official recommendations. There should be an interval of at least one month between doses.

Booster Vaccination

After primary series vaccination with either 2 doses (e.g., 3, 5 months) or 3 doses (e.g., 2, 3, 4 months) of PEDIACEL, a booster dose should be given at least 6 months after the last priming dose in accordance with applicable official recommendations.

PEDIACEL can be considered for the booster if the composition is in accordance with the applicable official recommendations.

Based on safety and immunogenicity data from clinical studies, PEDIACEL should preferably be given to children who received the same vaccine in infancy. However, PEDIACEL may be given as a booster to children who received other diphtheria, tetanus, pertussis, poliomyelitis and *Haemophilus influenzae* type b (Hib) with or without hepatitis B vaccines in their primary series.

Children less than 6 weeks of age: The safety and efficacy of PEDIACEL in children less than 6 weeks of age has not been established. No data are available

Children 4 years of age or older: The safety and efficacy of PEDIACEL in children 4 years of age or older has not been established. No data are available

Method of administration

PEDIACEL should be administered intramuscularly. The recommended injection sites are the anterolateral aspect of the thigh or the deltoid region of the upper arm if there is adequate muscle mass, according to local clinical practice recommendations. The anterolateral aspect of the thigh is the preferred site for infants under one year of age.

Do not administer PEDIACEL by intravascular injection; ensure that the needle does not penetrate a blood vessel. Do not administer subcutaneously.

Precautions to be taken before handling or administering the medicinal product

For instructions for preparation of the medicinal product before administration, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substances, to any of the excipients listed in section 6.1 or to any residual substances carried over from manufacture (neomycin, streptomycin, polymyxin B, glutaraldehyde, formaldehyde and bovine serum albumin), which may be present in undetectable trace amounts.

PEDIACEL is contraindicated if the infant has experienced an encephalopathy of unknown aetiology, occurring within

7 days following previous vaccination with pertussis containing vaccine. In these circumstances pertussis vaccination should be discontinued and the vaccination course should be continued with diphtheria, tetanus, polio and Hib vaccines.

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

As with other vaccines, administration of PEDIACEL should be postponed in children suffering from acute severe febrile illness. The presence of a minor infection (e.g., mild upper respiratory infection) is not a contraindication.

4.4 Special warnings and precautions for use

Applicable official recommendations for childhood immunizations should be consulted before administering this vaccine to children in or after the second year of life since the exact combination of antigens may not be considered appropriate and/or necessary after completion of the primary vaccination series.

Prior to immunization

As with all injectable vaccines, appropriate medical treatment and supervision should be readily available for immediate use in case of a rare anaphylactic reaction following the administration of the vaccine (see section 4.8).

If any of the following events have occurred after administration of a pertussis-containing vaccine, the decision to administer PEDIACEL should be based on careful consideration of potential benefits and possible risks.

• Temperature of ≥40°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.

If Guillain-Barré syndrome or brachial neuritis has occurred following receipt of prior vaccine containing tetanus toxoid, the decision to give any vaccine containing tetanus toxoid should be based on careful consideration of the potential benefits and possible risks.

A history of febrile convulsions, a family history of convulsions or Sudden infant death syndrome (SIDS) do not constitute a contraindication for the use of PEDIACEL. Vaccinees with a history of febrile convulsions should be closely followed up as such adverse events may occur within 2 to 3 days post vaccination.

The potential risk of apnoea 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.

Immunocompromised children (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. HIV infection is not considered as a contraindication. The expected immunological response may not be obtained after vaccination of immunosuppressed patients.

Administration precautions

As for all injectable products, the vaccine should be administered with caution to children with thrombocytopenia or bleeding disorders since bleeding may occur following an intramuscular injection.

Other considerations

As with any vaccine, a protective immune response may not be elicited in all vaccinees (see section 5.1).

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

influenzae or against meningitis of other origin.

Granuloma or sterile abscess at the injection site has been reported with vaccines containing aluminum.

Since the Hib capsular polysaccharide antigen is excreted in the urine, a positive urine test can be observed within 1-2 weeks following vaccination. Other tests should be performed in order to confirm Hib infection during this period.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant Vaccine Administration
PEDIACEL may be administered at the same time as, but as a separate injection to, any of the following monovalent or combination vaccines: hepatitis B, 7-valent pneumococcal conjugate, measles, mumps and rubella (MMR), varicella or meningococcal group C conjugate vaccines. Injections should be made into separate sites and, preferably, into separate limbs.

Meningococcal Group C Conjugate Vaccines
In a controlled clinical study PEDIACEL was administered concomitantly with two different meningococcal group C conjugate vaccines (a meningococcal group C CRM_{197} conjugate and a meningococcal group C tetanus toxoid conjugate vaccine) at 2, 3 and 4 months of age. Although seroprotection rates were high in both groups (>88.0% anti-PRP ≥0.15 micrograms/mL), antibody responses to the Hib component of PEDIACEL (PRP conjugated to tetanus toxoid) were lower when co-administered with a meningococcal group C CRM_{197} conjugate vaccine than with a meningococcal group C tetanus toxoid conjugate vaccine. PEDIACEL did not affect the proportions of infants with meningococcal group C serum bactericidal antibody (SBA) titres of at least 1:8 (measured with rabbit complement) when co-administered with either a CRM_{197} conjugate or a tetanus toxoid conjugate vaccine. (See Section 5.1.)

Vaccine/Drug Interactions
Immunosuppressive treatments may interfere with the development of the expected immune response. (See Section 4.4.)

4.6 Fertility, pregnancy and lactation

Not applicable. This vaccine is not intended for administration to women of child-bearing age.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

a. Summary of the Safety Profile

The data from 11 clinical trials conducted in several countries and using various immunization schedules were pooled. In these studies, PEDIACEL was administered in a primary series (N = 1487) and as a booster dose (N = 1632). The adverse reactions occurring after vaccination are summarised in Table 1 below.

The most frequently reported adverse reactions after PEDIACEL administration were decreased activity, injection site reactions (tenderness, erythema, swelling), pyrexia (≥38^{o}C), vomiting, abnormal crying, appetite loss, and irritability.

Adverse reactions spontaneously reported following the commercial use of PEDIACEL are also summarised in Table 1 below. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency.

b. Tabulated list of adverse reactions

Adverse reactions are ranked under headings of frequency using the following convention:
Very common (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1/1,000 to <1/100)
Rare (≥1/10,000 to <1/1,000)
Very Rare (<1/10,000), including individual cases
Not known: cannot be estimated from available data.

Table 1: List of Adverse Reactions

Adverse Reactions	**Frequency**
Immune System Disorders	
Hypersensitivity	Not known
Anaphylactic reaction (such as urticaria, angioedema).	
Metabolism and Nutrition Disorders	
Appetite loss	Very common
Psychiatric Disorders	
Irritability	Very common
Abnormal crying	Very common
Nervous System Disorders	
Convulsion (with or without fever)	Uncommon
High-pitched crying	Not known
*Hypotonic hyporesponsive episode (infant appears pale, hypotonic (limp) and unresponsive).	
Somnolence	
Vascular Disorders	
Pallor	Not known
Respiratory, Thoracic and Mediastinal Disorders	
Apnoea	Not known
Gastrointestinal Disorders	
Vomiting	Very common
Diarrhoea	Common
Skin and Subcutaneous Tissue Disorders	
Rash	Not known
Musculoskeletal, Connective Tissue and Bone Disorders	
Pain in vaccinated limb	Not known
General Disorders and Administration Site Conditions	
Decreased activity	Very common
Injection site tenderness	
Injection site erythema	
Pyrexia (≥38°C),	
Injection site swelling	
Injection site bleeding	Common
Injection site bruising	
Extensive limb swelling (from the injection site beyond one or both joints)	Uncommon

Pyrexia (>40.5°C),	Not known
Injection site mass	
Asthenia	
Listlessness	
Edematous reactions affecting one or both lower limbs	

* To date, this condition has not been associated with any permanent sequelae.

c. Description of selected adverse reactions

Edematous reactions affecting one or both lower limbs have occurred following vaccination with *H. 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. All events resolved spontaneously without sequelae within 24 hours.

d. Other Special Populations

Apnoea in very premature infants (≤28 weeks of gestation). (See section 4.4)

4.9 Overdose

Not applicable.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Bacterial and viral vaccines combined, diphtheria-haemophilus influenzae B-pertussis-poliomyelitis-tetanus, ATC code J07CA06.

Immunogenicity

In a randomized, single-blind, controlled multi-centre clinical trial, the immunogenicity of PEDIACEL was compared to another DTaP-IPV+Hib vaccine when administered to infants using the three-dose primary immunization schedule of 2, 3 and 4 months with a booster dose given at 12-18 months. Antibody responses one month after completion of the three-dose primary series and one month after the booster dose of PEDIACEL are summarized below.

Table 2: Immune Responses

Antigen	**Criteria**	**PEDIACEL Post-dose 3 N = 248**	**PEDIACEL Post-dose 4 N = 220**
Diphtheria	≥0.01 IU/mL ≥0.1 IU/mL	99.2% 39.3%	-- 99.1%
Tetanus	≥0.01 IU/mL ≥0.1 IU/mL	100.0% 99.2%	-- 100.0%
Pertussis Pertussis Toxoid Filamentous Haemagglutinin Pertactin Fimbriae Types 2 and 3	 seroresponse* seroresponse† seroresponse* seroresponse*	 98.7% 93.2% 87.5% 95.8%	 96.7% 83.2% 86.9% 95.7%
Polio Type 1	 ≥1:8 Dilution	 100.0%	 99.5%

Type 2 Type 3	≥1:8 Dilution ≥1:8 Dilution	99.2% 99.6%	99.5% 99.5%
Haemophilus influenzae type b PRP	≥0.15 micrograms/mL ≥1.0 micrograms/mL	91.0% 63.3%	-- 99.1%

* Post-dose 3 ≥4 EU/mL if pre-dose 1 <4 EU/mL or post-dose 3 ≥ pre-dose 1 if pre-dose 1 ≥4 EU/mL. Four-fold rise from pre-dose 4 if pre-dose 4 <4 x 4 EU/mL or two-fold rise from pre-dose 4 ≥4 x 4 EU/mL.

† Post-dose 3 ≥3 EU/mL if pre-dose 1 <3 EU/mL or post-dose 3 ≥ pre-dose 1 if pre-dose 1 ≥3 EU/mL. Four-fold rise from pre-dose 4 if pre-dose 4 <4 x 3 EU/mL or two-fold rise from pre-dose 4 if pre-dose 4 ≥4 x 3 EU/mL.

In a controlled clinical trial, the immunogenicity of booster vaccination with PEDIACEL was compared to a hexavalent DTaP-IPV-Hib-Hepatitis B vaccine given at 11 to 18 months of age in toddlers who had been primed with 3 doses of DTaP-IPV-Hib-Hepatitis B vaccine. 100% of participants receiving PEDIACEL achieved seroprotective levels for diphtheria and tetanus (≥0.1 IU/mL), PRP (≥1.0 micrograms/mL) and all three types of polio (≥1:8 dilution). The booster response rates for pertussis antigens PT, FHA, PRN and FIM were 90.4%, 86.7%, 95.9% and 26.4%. This was the first dose containing FIM for these participants.

In a randomized, double-blind, controlled clinical trial, the immunogenicity of PEDIACEL was compared to another DTaP-IPV+Hib vaccine when administered to infants using the two-dose primary immunization schedule of 3 and 5 months followed by a booster dose at 12 months. Antibody responses one month after completion of the three-dose series are summarized below.

Table 3: Immune Response

Antigen	**Criteria**	**PEDIACEL Post-dose 3 N = 325**
Diphtheria	≥0.01 IU/mL ≥0.1 IU/mL	98.2% 95.1%
Tetanus	≥0.01 IU/mL ≥0.1 IU/mL	100.0% 100.0%
Pertussis Pertussis Toxoid Filamentous Haemagglutinin Pertactin Fimbriae Types 2 and 3	 seroresponse* seroresponse† seroresponse* seroresponse*	 98.5% 99.1% 96.9% 96.3%
Polio Type 1 Type 2 Type 3	 ≥1:8 Dilution ≥1:8 Dilution ≥1:8 Dilution	 99.4% 99.7% 98.8%
Haemophilus influenzae type b PRP	≥0.15 micrograms/mL ≥1.0 micrograms/mL	99.1% 93.2%

* Post-dose 3 ≥4 EU/mL if pre-dose 1 <4 EU/mL or post-dose 3 ≥ pre-dose 1 if pre-dose 1 ≥4 EU/mL.

† Post-dose 3 ≥3 EU/mL if pre-dose 1 <3 EU/mL or post-dose 3 ≥ pre-dose 1 if pre-dose 1 ≥3 EU/mL.

Pertussis efficacy

In a clinical trial in Sweden (Sweden I Efficacy Trial), the pertussis components in PEDIACEL (i.e., PT, FHA, PRN and FIM) have been shown to prevent pertussis in infants with a protective efficacy of 85.2% using the WHO case definition (≥21 consecutive days of paroxysmal cough with culture or serologic confirmation or epidemiological link to a confirmed case). In the same study, the protective efficacy against mild disease (≥1 day of paroxysmal cough with culture or serologic confirmation) was 77.9%. In a controlled clinical trial in Sweden (Sweden II Trial), a DTaP

vaccine with the same formulation of pertussis antigens as PEDIACEL demonstrated protection against pertussis with any cough.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Limited pre-clinical testing of PEDIACEL and closely related products revealed no unexpected findings and no target organ toxicity.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Phenoxyethanol
Polysorbate 80
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, PEDIACEL must not be mixed with other medicinal products.

6.3 Shelf life

4 years

6.4 Special precautions for storage

Store in a refrigerator (2°C - 8°C). **Do not freeze**. Keep the container in the outer carton in order to protect from light.

6.5 Nature and contents of container

0.5 mL of suspension in pre-filled syringe (type I glass) with a plunger stopper (halobutyl elastomer), without attached needle, with a tip-cap (halobutyl elastomer) - pack size of 1, 10 or 20.

0.5 mL of suspension in pre-filled syringe (type I glass) with a plunger stopper (halobutyl elastomer), without attached needle, with a tip-cap (halobutyl elastomer) and 2 separate needles - pack size of 1 or 10.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Instructions for Use

The vaccine should be used as supplied; no dilution or reconstitution is necessary.

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

Shake the pre-filled syringe well to uniformly distribute the suspension before administering the vaccine. The normal appearance of the vaccine is a uniform, cloudy, white to off-white suspension, which may sediment during storage.

The needle should be pushed firmly on to the end of the pre-filled syringe and rotated through 90 degrees.

Disposal

Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Sanofi Pasteur MSD Ltd
Block A, Second Floor
Cookstown Court
Old Belgard Road
Tallaght
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER

PA 544/41/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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