SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

PNEUMOSIL

Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (10-Valent) 1 Dose

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Name of the ingredient	Target conc./dose	Reference to pharmacopoeia	Functional role
Active Ingredients*			
Saccharide for each serotype 1,5, 6A, 7F, 9V, 14, 19A, 19F and 23F	2 µg	IP/BP /WHO /IH	Pneumococcal Serotype
Saccharide for serotype 6B	4 µg	IP/BP /WHO/ IH	
Inactive Ingredients			
Aluminium (as Aluminium phosphate)	0.125 mg[#] Al^{+++}	IH	Adjuvant

*The active ingredients of the vaccine are conjugated to a carrier protein rCRM197 (In-house)

[#]Theoretical quantities.

IP: Indian Pharmacopoeia, **BP:** British Pharmacopoeia, **Ph. Eur:** European Pharmacopoeia,
WHO: World Health Organization (TRS 977, Annex 3)
IH: Manufacturer's In-house specifications.

3 PHARMACEUTICAL FORM

Suspension for injection.
Whitish turbid liquid.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

- Active immunization against invasive disease, pneumonia and acute otitis media caused by *Streptococcus pneumoniae* serotypes 1, 5, 6A, 6B, 7F, 9V, 14, 19A, 19F and 23F in infants and toddlers from 6 weeks up to 2 years of age.
- The use of vaccine should be determined based on relevant recommendations and take into consideration the disease impact by age and regional epidemiology.

4.2 Posology and method of administration

4.2.1 Preparation for Administration:

The dose is 0.5 ml given intramuscularly, with care to avoid Injection into or near nerves and blood vessels. The vaccine should be given by intramuscular injection. The preferred sites are anterolateral aspect of the thigh in infants or the deltoid muscle of the upper arm in young

children. The vaccine should not be injected in the gluteal area. Do not administer Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (10-valent) intravascularly. The vaccine should not be injected intradermally, subcutaneously or intravenously since the safety and immunogenicity of these routes have not been evaluated.

4.2.2 Administration information

For intramuscular injection only.

The preferred sites are anterolateral aspect of the thigh in infants or the deltoid muscle of the upper arm in young children. The vaccine should not be injected in the gluteal area. Do not administer Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (10-valent) intravascularly. The vaccine should not be injected intradermally, subcutaneously or intravenously since the safety and immunogenicity of these routes have not been evaluated.

4.2.3 Vaccination schedule

Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (10-valent) is to be administered as a three-dose primary series at 6, 10, and 14 weeks of age or 2, 3 and 4 months of age or 2, 4 and 6 months of age, with or without, depending on recommended dosing schedule, a booster dose at 9-10 or 12-15 months of age. The minimum interval between doses should be 4 weeks. If a booster dose is given, it should be at least 6 months after the last primary dose.

Table 1: Vaccination Schedules for Infants and Toddlers

Dosage Schedules	Dose 1[a,b]	Dose[2b]	Dose[3b]	Dose[4c]
3p+1	6 weeks	10 weeks	14 weeks	9 – 10 months or 12-15 months
3p+0	6 weeks	10 weeks	14 weeks	

[a] Dose 1 may be given as early as 6 weeks or at 2 months of age

[b] The recommended dosing interval is 4 to 8 weeks

[c] A booster (fourth) dose is recommended at least 6 months after the last primary dose and may be given from the age of 9 months onwards (preferably between 12 and 15 months of age)

For children who are beyond the age of routine infant schedule, the following Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (10-valent) schedule is proposed:

The catch-up schedule, for children 7 months through 2 years of age who have not received Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (10-valent):

Table 2: Vaccination Schedules for Unvaccinated Children 7 Months of Age Through 2 Years of Age	
Age at first dose	**Total Number of 0.5 ml doses**
7-11 months of age	3a
12-24 months of age	2b

[a] The vaccination schedule consists of two primary doses of 0.5 ml with an interval of at least 1 month between doses. A booster (third) dose is recommended in the second year of life with an interval of at least 2 months after the last primary dose.

[b] The vaccination schedule consists of two doses of 0.5 ml with an interval of at least 2 months between doses.

4.3 Contraindications

Hypersensitivity to any component of the vaccine, including diphtheria toxoid.

4.4 Special warnings and precautions for use

As with all injectable vaccines, appropriate medical treatment and supervision must always be readily available in case of a rare anaphylactic event following the administration of the vaccine.

PRECAUTIONS

ADRENALINE INJECTION (1:1000) MUST BE IMMEDIATELY AVAILABLE SHOULD AN ACUTE ANAPHYLACTIC REACTION OCCUR DUE TO ANY COMPONENT OF THE VACCINE.

For treatment of severe anaphylaxis, the initial dose of adrenaline is 0.1- 0.5 mg (0.1- 0.5 ml of 1:1000 injection) given s/c or i/m.

Single dose should not exceed 1 mg (1 ml). For infants and children, the recommended dose of adrenaline is 0.01 mg/kg (0.01 ml/kg of 1:1000 injection). Single pediatric dose should not exceed 0.5 mg (0.5 ml). The mainstay in the treatment of severe anaphylaxis is the prompt use of adrenaline, which can be lifesaving. It should be used at the first suspicion of anaphylaxis.

As with the use of all vaccines the vaccinee should remain under observation for not less than 30 minutes for possibility of occurrence of immediate or early allergic reactions. Hydrocortisone and antihistaminics should also be available in addition to supportive measures such as oxygen inhalation and IV fluids.

Special care should be taken to ensure that the injection does not enter a blood vessel.

IT IS EXTREMELY IMPORTANT WHEN THE PARENT, GUARDIAN RETURNS FOR THE NEXT DOSE IN THE SERIES, THE PARENT, and GUARDIAN SHOULD BE QUESTIONED CONCERNING OCCURRENCE OFANY SYMPTOMSAND/OR SIGNS OFANADVERSE REACTIONAFTER THE PREVIOUS DOSE.

Minor illnesses, such as mild respiratory infection, with or without low grade fever, are not generally contraindications to vaccination. The decision to administer or delay vaccination because of a current or recent febrile illness depends largely on the severity of the symptoms and their etiology. The administration of Pneumococcal
Polysaccharide Conjugate Vaccine (Adsorbed) (10-valent) should be postponed in subjects suffering from acute severe febrile illness. As with any intramuscular injection, Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (10-valent) should be given with, caution to infants or children with thrombocytopenia or any coagulation disorder, or to those receiving anticoagulant therapy. This vaccine is not intended to be used for treatment of active infection. As with any vaccine,
Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (10-valent) may not protect all individuals receiving the vaccine from pneumococcal disease.

SPECIAL POPULATIONS:

Safety and immunogenicity data on Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (10-valent) are not available for children in specific groups at higher risk for invasive pneumococcal disease (e.g., children with congenital or acquired splenic dysfunction, HIV infection, malignancy, nephrotic syndrome). Children in these groups may have reduced antibody response to active immunization due to impaired immune responsiveness. Limited data have demonstrated that other pneumococcal conjugate vaccines induce an immune response in children with HIV, sickle cell disease, and children born prematurely with a safety profile similar to that observed in non- high-risk groups. The use of Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (10-valent) in high-risk groups should be considered on an individual basis.

Apnoea in Premature Infants: Based on experience with use of other pneumococcal conjugate vaccines, the potential risk of apnoea and the need for respiratory monitoring for 48-72h 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 with Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (10-valent) should not be withheld or delayed. Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) I.P. (10-valent) is not intended for use in children below the age of 6 weeks. The safety and effectiveness in children below the age of 6 weeks has not been established.

4.5 Interaction with other medicinal products and other forms of interaction

Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (10-valent) can be given with any of the following vaccine antigens, either as monovalent or combination vaccines: diphtheria, tetanus, whole-cell pertussis, Haemophilus influenzae type b, inactivated or oral poliomyelitis, rotavirus, yellow fever, hepatitis B, measles, and rubella. Clinical studies demonstrated that the immune responses and the safety profiles of the administered vaccines were unaffected. Studies with other pneumococcal conjugate vaccines co-administered with mumps, varicella, meningococcal ACWY, and rotavirus vaccines have demonstrated that the immune responses of the other pneumococcal conjugate vaccines and the co-administered vaccines were unaffected.

In clinical trials, when other pneumococcal conjugate vaccines were given concomitantly but at a different site/route, with rotavirus vaccine or hepatitis A vaccine, no change in the safety profiles for these infants was observed. Different injectable vaccines should always be given at different injection-sites. Till date Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (10-valent) clinical studies have been conducted in India and The Gambia in toddlers and infants. In the Gambia Phase 1/2 study, there was no evidence that administration of Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (10-valent) interfered with the immune response to any component of co-administered pentavalent vaccine. In the Gambia Phase 3 study, non-inferiority of the immune responses induced by EPI vaccines between treatment groups was demonstrated for all EPI vaccines co-administered during the 3-dose primary vaccination series (6 weeks, 10 weeks and 14 weeks) – namely, whole-cell pentavalent vaccine (DTwP-HepB-Hib) oral polio vaccine, inactivated polio vaccine, and oral rotavirus vaccine. Standard EPI vaccines based on the Gambian EPI schedule (measles-rubella vaccine and yellow fever virus vaccine) were co- administered with the booster dose of study vaccine. Non-inferiority of the immune responses was demonstrated for these co-administered EPI vaccines. While there are no known published data on co-administration of other pneumococcal conjugate vaccine with yellow fever virus vaccine, the high seroresponse rate to yellow fever in the Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (10- valent) group indicates that Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (10-valent) does not interfere with the immune response to yellow fever virus vaccine.
This section will continue to be updated along with further studies.

4.6 Fertility, pregnancy and lactation
Human data on the use during pregnancy or breast-feeding or lactation and animal reproduction studies are not available.

4.7 Effects on ability to drive and use machines
Not relevant.

4.8 Undesirable effects
Summary of the safety profile
Safety assessment of Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed)
(10-valent) was based on clinical trials involving the administration of 5,187 doses to 1,603 healthy children as primary immunization. Furthermore, 428 children received a booster dose of Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (10-valent) following a primary vaccination course. Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (10-valent) was administered concomitantly with recommended childhood vaccines, as appropriate.
Safety was also assessed in 57 previously unvaccinated children during the second year of life; all children received 2 doses of vaccine. Pneumococcal Polysaccharide Conjugate

Vaccine (Adsorbed) (10-valent) has also been used for booster vaccination in 56 children who received another pneumococcal conjugate vaccine for the primary course.

The vast majority of the reactions observed following vaccination were of mild or moderate severity and were of short duration.

In the largest study in infants, the most common adverse reactions observed after primary vaccination were tenderness at the injection site, fever, and irritability, which were reported for approximately 49%, 52%, and 32% of all infants, respectively. No increase in the incidence or severity was observed following subsequent doses of the primary vaccination course. Following booster vaccination, the most common adverse reaction was tenderness at the injection site, which was reported for approximately 8% of all infants.

The injection site and systemic reactions following catch-up vaccination or booster vaccination during the second year of life were similar to those reported after primary vaccination.

In all studies, the incidence and severity of local and general adverse reactions reported within 7 days of vaccination were similar to those after vaccination with the licensed comparator PCV.

Tabulated list of adverse reactions

Adverse reactions (i.e. events considered as related to vaccination) have been categorised by frequency for all age groups.

Frequencies are reported as:

Very common (≥1/10 vaccinees)

Common (≥1/100 vaccinees but < 1/10 vaccinees)

Uncommon (≥1/1000 vaccinees but < 1/100 vaccinees)

Rare (≥1/10,000 vaccinees but < 1/1,000 vaccinees)

System Organ Class	Frequency	Adverse reactions
Gastrointestinal disorders	Uncommon	Diarrhoea
General disorders and administration site conditions	Very common	Pain, Fever ≥ 37.5°C (axillary)
	Common	Erythema, swelling/induration
	Uncommon	Fever > 39°C (axillary)
Metabolism and nutrition disorders	Common	Decreased appetite
Nervous system disorders	Common	Drowsiness
Psychiatric disorders	Very common	Irritability
Skin and subcutaneous tissue disorders	Common	Rash

4.9 Overdose

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vaccines

Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (10-Valent)

ATC code J07AL02.

Mode of Action: PNEUMOSIL (10-valent) is a pneumococcal polysaccharide conjugate vaccine containing 10 pneumococcal capsular polysaccharides (1, 5, 6A, 6B, 7F, 9V, 14, 19A, 19F, 23F) that are conjugated via CDAP chemistry to a genetically recombinantly-derived carrier protein, CRM197. T-dependent and T-independent mechanistic pathways both come into play in the production of antibodies by B cells stimulated by antigens. Helper T cell (CD4+ T cell) mediated signals to B cells through surface protein engagement and cytokine release causes them to proliferate and differentiate into long-lived plasma cells that keep producing IgG antibodies (among other isotypes), and memory B cells that are primed to produce antibodies whenever re-exposed to the same antigen. Capsular polysaccharides, however, only work via the T-independent pathway, causing B cells recruited to only largely produce IgM antibodies, with no affinity maturation, and no proliferation and differentiation into memory B cells either. Unconjugated polysaccharide vaccines therefore are very poorly (to not at all) immunogenic in infants and toddlers (children under the age of 2 years) and fail in the induction of immune memory at any and all ages as well. It is therefore necessary to conjugate the T-independent capsular polysaccharides to an immunogenic T-dependent protein carrier (like CRM197) to recruit the T-dependent pathway that then results in B cell antibody affinity maturation and the induction of long-term immune memory via the proliferation of memory B cells, eliciting then strong boosting in infants and younger children when challenged with the same pneumococcal capsular polysaccharides later in life.

Immunological Data:

Clinical trials performed to assess immunogenicity and reactogenicity of the vaccine and proved that the vaccine is immunogenic.

5.2 Pharmacokinetic properties

Pharmacokinetic studies are not required for vaccines.

5.3 Preclinical safety data

Single and multiple administration of the Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (10-valent) to rats and rabbits were well tolerated and revealed no evidence of any significant local or systemic toxic effects. Observed changes were not considered adverse but rather a consequence of the pharmacological activity of Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (10-valent) and licensed pneumococcal conjugate vaccine comparator.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Aluminium Phosphate gel 2%
L-Histidine
Succinic acid
Sodium Chloride
Water for injection (WFI)
Polysorbate-20
Sodium Hydroxide
Hydrochloric Acid

6.2 Incompatibilities

The vaccine is not to be mixed with other vaccines/products in the same syringe.

6.3 Shelf life

36 months from the date of manufacturing.

6.4 Special precautions for storage

Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (10-valent) should be stored at 2 - 8° C. DO NOT FREEZE. Discard if the vaccine has been frozen.

6.5 Nature and contents of container

Single dose presentation: 1 dose vial of 0.5 ml

6.6 Special precautions for disposal and other handling

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

requirements.

7. MARKETING AUTHORISATION HOLDER

SERUM INSTITUTE OF INDIA PVT. LTD.
212/2, Hadapsar, Pune 411028, INDIA

8. MARKETING AUTHORISATION NUMBER(S)

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9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10. DATE OF REVISION OF THE TEXT

12/2019