Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed)

(10-Valent)

DESCRIPTION:

Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (10-valent) is a sterile suspension of saccharides of the capsular antigens of *Streptococcus pneumoniae* serotypes 1, 5, 6A, 6B, 7F, 9V, 14, 19A, 19F and 23F individually conjugated by using 1-cyano-4-dimethylamino pyridinium tetrafluoroborate chemistry (CDAP) to non-toxic diphtheria CRM197 protein. The polysaccharides are chemically activated and then covalently linked to the protein carrier CRM197 to form the glycoconjugate. Individual conjugates are compounded and then polysorbate 20 and aluminium phosphate are added to formulate the vaccine. The potency of the vaccine is determined by the quantity of the saccharide antigens and the saccharide-to-protein ratios in the individual glycoconjugates. The vaccine meets the requirements of WHO, IP and BP when tested by the methods outlined in WHO TRS 977, IP and BP.

COMPOSITION:

Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (10-Valent) 0.5 ml - 1 dose

Each dose of 0.5 ml contains:

Saccharide for serotypes 1, 5, 9V, 14, 19A, 19F, 23F, 7F, 6A	2 mcg each
Saccharide for serotype 6B	4 mcg
Conjugated to CRM197 carrier protein	19 to 48 mcg
Aluminium (as Aluminium phosphate)	0.125 mg

Dose : 0.5 ml by intramuscular injection.

Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (10-Valent) 2.5 ml - 5 dose

Each dose of 0.5 ml contains:

Saccharide for serotypes 1, 5, 9V, 14, 19A, 19F, 23F, 7F, 6A	2 mcg each
Saccharide for serotype 6B	4 mcg
Conjugated to CRM197 carrier protein	19 to 48 mcg
Aluminium (as Aluminium phosphate)	0.125 mg
Thiomersal:	0.005 %

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 on the basis of relevant recommendations and take into consideration the disease impact by age and regional epidemiology.

DOSAGE AND ADMINISTRATION: For Intramuscular use only :

The dose is 0.5 ml given intramuscularly, with care to avoid Injection into or near nerves and blood vessels. The product is a suspension containing an adjuvant, shake vigorously immediately prior to use to obtain a homogenous, whitish turbid liquid in the vaccine container. 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.
Once opened, multi-dose vials should be kept between +2°C and +8°C. Multi-dose vials of Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (10-valent) from which one or more doses of vaccine have been removed during an immunization session may be used in subsequent immunization sessions for up to a maximum of 28 days, provided that all of the following conditions are met (as described in the WHO policy statement: Handling of multi-dose vaccine vials after opening, WHO/IVB/14.07):

- The vaccine is currently prequalified by WHO;
- The vaccine is approved for use for up to 28 days after opening the vial, as determined by WHO;
- The expiry date has not passed;
- The vaccine vial has been, and will continue to be, stored at WHO - or manufacturer recommended temperatures; furthermore, the vaccine vial monitor, if one is attached, is visible on the vaccine label and is not past its discard point, and the vaccine has not been damaged by freezing.

The vaccine should be visually inspected for any foreign particulate matter and / or variation of physical aspect prior to administration. In event of either being observed, discard the vaccine.

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 Schedule for Infants and Toddlers

Dosage Schedules	Dose 1 [a, b]	Dose 2 [b]	Dose 3 [b]	Dose 4 [c]
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	3[a]
12-24 months of age	2[b]

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.

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

SPECIAL WARNINGS:
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 OF ANY SYMPTOMS AND/OR SIGNS OF AN ADVERSE REACTION AFTER 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 48-72 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 with Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (10-valent) should not be withheld or delayed.

PREGNANCY & LACTATION:
Human data on the use during pregnancy or lactation are not available.

PEDIATRIC USE:
Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (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.

INTERACTIONS:
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 ½ 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.

ADVERSE REACTIONS:
Summary of the safety profile
Safety assessment of Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (10-valent) was based on clinical trials involving the administration of 5,416 doses to 1,828 healthy children as primary immunisation. 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 Indian Phase 3 licensure study in infants similarly showed tenderness at the injection site, fever and irritability as the most common adverse reactions observed after primary vaccination, with no change in the incidence or severity observed following subsequent doses of the primary vaccination course. Majority of the solicited AEs were of mild to moderate intensity and resolved completely.
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

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.

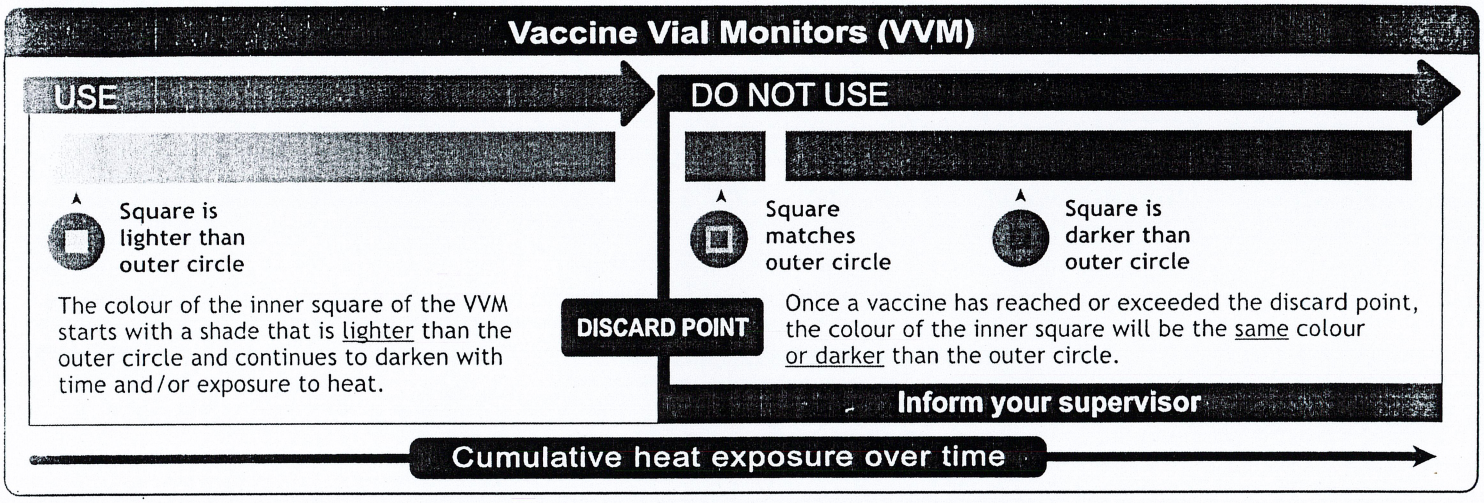
COMPATIBILITIES, INCOMPATIBILITIES:
The vaccine is not to be mixed with other vaccines/products in the same syringe.

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. A fine white deposit with clear colourless supernatant may be observed upon storage of the vial. This does not constitute a sign of deterioration.

SHELF LIFE:
36 months from the date of manufacture.

PRESENTATION:
1 dose - 0.5 ml vial
5 dose - 2.5 ml vial

THE VACCINE VIAL MONITOR (VVM) (Optional)



Vaccine Vial Monitors (VVMs) are on the cap of the vial / part of the label on Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (10-valent) supplied through Serum Institute of India Pvt. Ltd. This is a time-temperature sensitive dot that provides an indication of the cumulative heat to which the vial has been exposed. It warns the end user when exposure to heat is likely to have degraded the vaccine beyond an acceptable level.

The interpretation of the VVM is simple. Focus on the central square. Its colour will change progressively. As long as the colour of this square is lighter than the colour of the outer circle, then the vaccine can be used. As soon as the colour of the central square is the same colour as the outer circle or of a darker colour than the outer circle, then the vial should be discarded.

Revision date: 01/2021

Manufactured by:
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Protection from birth onwards

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