MODULE 1.3.1.1 PROPOSED PROFESSIONAL INFORMATION FOR PCV-10 CIPLA

SCHEDULING STATUS

S2

1. NAME OF MEDICINE

PCV-10 CIPLA Suspension for injection

Pneumococcal polysaccharide conjugate vaccine (10-valent, adsorbed)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 0,5 mL (1 dose) suspension for injection contains:

Pneumococcal polysaccharide serotype 1: 2 mcg;

Pneumococcal polysaccharide serotype 5: 2 mcg;

Pneumococcal polysaccharide serotype 6A: 2 mcg;

Pneumococcal polysaccharide serotype 6B: 4 mcg[)];

Pneumococcal polysaccharide serotype 7F: 2 mcg;

Pneumococcal polysaccharide serotype 9V: 2 mcg;

Pneumococcal polysaccharide serotype 14: 2 mcg;

Pneumococcal polysaccharide serotype 19A: 2 mcg;

Pneumococcal polysaccharide serotype 19F: 2 mcg; and

Pneumococcal polysaccharide serotype 23F: 2 mcg.

Serotypes are conjugated to CRM197-diphtheria carrier protein 19 to 48 mcg, adsorbed on aluminium phosphate. Each 0,5 mL dose contains 0,125 mg aluminium. Sugar free.

For the full list of excipients, see **section 6.1**.

3. PHARMACEUTICAL FORM

Suspension for injection.

PCV-10 CIPLA is a whitish turbid liquid (filled in clear glass vials closed with rubber closure, aluminum seal and a polypropylene flip-off cap) tends to settle down on keeping and is free from foreign particles/floccules.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Active immunisation 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.

4.2. Posology and method of administration

PCV-10 CIPLA is given intramuscularly, with care to avoid injection into or near nerves and blood vessels. PCV-10 CIPLA is a suspension containing an adjuvant, it must be shaken vigorously immediately prior to use to obtain a homogenous, whitish turbid suspension in the vaccine container.

PCV-10 CIPLA 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:

PCV-10 CIPLA is to be administered as a three-dose primary series at dosing schedule from six weeks of age. A booster dose is to be administered 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 to 10 months or 12 to 15 months
3p + 0	6 weeks	10 weeks	14 weeks	

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

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

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

For children who are beyond the age of routine infant schedule, the following schedule is proposed:

The catch-up schedule, for children aged 7 to 24 months who have not received PCV-10 CIPLA is as follows:

Table 2: Vaccination schedule for unvaccinated children aged 7 to 24 months of age

Dosage schedules	**Total number of 0,5 mL doses**
7 to 11 months	3[a]
12 to 24 months	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.

Method of administration:

PCV-10 CIPLA 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 PCV-10 CIPLA intravascularly. The vaccine should not be injected intradermally, subcutaneously or intravenously, since the safety and immunogenicity of these routes have not been evaluated.

4.3. Contraindications

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

4.4. Special warnings and precautions for use

Appropriate medical treatment and supervision must always be readily available in case of a rare anaphylactic event following the administration of the vaccine. Hydrocortisone and antihistaminics should also be available in addition to supportive measures such as oxygen inhalation and IV fluids.

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

VACCINE. 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.
Special care should be taken to ensure that the injection does not enter a blood vessel (see **section 4.2**). 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 aetiology. The administration of PCV-10 CIPLA should be postponed in subjects suffering from acute severe febrile illness. As with any intramuscular injection, PCV-10 CIPLA should be given with, caution to infants or children with thrombocytopenia or any coagulation disorder, or to those receiving anticoagulant therapy. PCV-10 CIPLA is not intended to be used for treatment of active infection. As with any vaccine, PCV-10 CIPLA may not protect all individuals receiving the vaccine from pneumococcal disease.

Safety and immunogenicity data on PCV-10 CIPLA 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 immunisation 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 PCV-10 CIPLA 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 immunisation 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 PCV-10 CIPLA should not be withheld or delayed.

4.5. Interactions with other medicines and other forms of interaction

PCV-10 CIPLA 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 PCV-10 CIPLA clinical studies have been conducted in India and The Gambia in toddlers and infants. In the Gambia Phase I/II study, there was no evidence that administration of PCV-10 CIPLA 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 sero-response rate to yellow fever in the PCV-10 CIPLA group indicates PCV-10 CIPLA does not interfere with the immune response to yellow fever virus vaccine.

4.6. Fertility, pregnancy and lactation

There are no data on pregnancy and breastfeeding.

4.7. Effects on ability to drive and use machines

Data on “Effects on ability to drive and use machines” are not available.

4.8. Undesirable effects

Summary of safety profile:

Safety assessment of PCV-10 CIPLA was based on clinical trials involving the administration of 5416 doses to 1828 healthy children as primary immunisation. Furthermore, 428 children received a booster dose of PCV-10 CIPLA following a primary vaccination course. PCV-10 CIPLA 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. PCV-10 CIPLA 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 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.

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 (≥1/1 000 vaccinees but < 1/100 vaccinees)
- Rare (≥1/10 000 vaccinees but < 1/1 000 vaccinees)

Infections and infestation:

Very common: upper respiratory tract infection.

Immune system disorders:

Frequency not known: anaphylaxis (see **section 4.4**)

Metabolism and nutrition disorders:

Common: decreased appetite.

Psychiatric disorders:

Very common: irritability.

Nervous system disorders:

Common: drowsiness.

Gastrointestinal disorders:

Uncommon: diarrhoea.

General disorders and administration site conditions:

Very common: pain, fever > 37,5 °C.

Common: erythema, swelling/ induration

Uncommon : fever > 39 °C

Skin and subcutaneous tissue disorders:

Common: rash.

Reporting of suspected adverse reactions

If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the "6.04 Adverse Drug Reaction Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of PCV-10 CIPLA. You may also report any suspected side effects (to Cipla Medpro (Pty) Ltd) by e-mail: drugsafetysa@cipla.com or telephone: 080 222 6662 (toll free).

4.9. Overdose

In overdose, side effects can be precipitated and/or be of increased severity. (see **section 4.8**)

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: A.30.1 – Biological antigens

ATC code: J07AL02

PCV-10 CIPLA contains polysaccharides corresponding to the 10 most prevalent IPD-causing serotypes in Africa, Asia, and Latin America, based on surveillance studies conducted prior to the introduction of PCVs in these regions.

Unconjugated polysaccharides are poorly immunogenic in infants less than 2 years old and do not induce long-term immune memory in recipients of any age. Conjugation of polysaccharides to an immunogenic protein carrier (as contained in PCV-10 CIPLA) overcomes the T cell-independent nature of polysaccharide antigens. In addition to a B-cell response, polysaccharide-protein conjugates also generate carrier protein-specific T helper cells, which provide the signals needed for B-cell maturation and memory B-cell generation. Thus, protein conjugation is expected to enhance the antibody response to each serotype, induce immune memory, and elicit an anamnestic response when immunised infants and young children are re-exposed to pneumococci.

5.2. Pharmacokinetic properties

Evaluation of pharmacokinetic properties is not available for vaccines.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

- Aluminium phosphate
- L-Histidine
- Polysorbate-20
- Sodium chloride
- Succinic acid
- Water for Injection

6.2. Incompatibilities

PCV-10 CIPLA must not be mixed with other medicines.

6.3. Shelf life

36 months.

6.4. Special precautions for storage

PCV-10 CIPLA must be stored at 2 °C to 8 °C, in the refrigerator.

Shake well.

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. The does not constitute a sign of deterioration.

6.5. Nature and contents of container

PCV-10 CIPLA is marketed in a mono-carton pack or packs of 50’s in clear or amber, tubular glass vials that are fitted with grey rubber stoppers containing an aluminium seal with polypropylene flip-top cap, that are packed into an outer carton.

6.6. Special precautions for disposal and other handling

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

7. HOLDER OF CERTIFICATE OF REGISTRATION

CIPLA MEDPRO (PTY) LTD

Building 9, Parc du Cap,

Mispel Street,

Belville, 7530,

RSA

Company Contact Details

Phone: +27 21 943 4200

Customer Care: 080 222 6662

E-mail: info@cipla.com

8. REGISTRATION NUMBER(S)

TBC

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

TBC

10. DATE OF REVISION OF THE TEXT

Not applicable.