PROFESSIONAL INFORMATION FOR

CIHEXA

SCHEDULING STATUS

S2

1. NAME OF THE MEDICINE

CIHEXA - Diphtheria, tetanus, *Bordetella pertussis* (whole cell), hepatitis B (rDNA), poliomyelitis (inactivated) and *Haemophilus influenzae* type b conjugate vaccine (adsorbed). Suspension for injection.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each single dose of 0,5 mL contains:

Name of the active ingredients	**Quantity for 0,5 mL single dose**
Diphtheria toxoid	≥ 30 IU
Tetanus toxoid	≥ 40 IU
Bordetella pertussis (whole cell)	≥ 4 IU
Hepatitis B Surface Antigen (rDNA)	15 mcg
Inactivated polio vaccine (Salk strains grown on vero cells) Type I (Mahoney strain) Type 2 (MEF-1 strain) Type 3 (Saukett strain)	 40 DU 8 DU 32 DU
Haemophilus influenzae type b (PRP) Conjugate to Tetanus toxoid (carrier protein)	10 mcg 19 to 33 mcg

Sugar free.

Contains preservative: 2-Phenoxyethanol 0,5 %

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

3. PHARMACEUTICAL FORM

Suspension for injection, presented in a single-dose vial and 10-dose vial (multi dose).

Pinkish to yellowish turbid liquid in which the mineral carrier (aluminium phosphate adjuvant) tends to settle down slowly on keeping and is free from foreign particles/ floccules.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

CIHEXA is indicated for active immunisation of infants, at or above the age of 6 weeks against diphtheria, tetanus, *Bordetella pertussis*, hepatitis B, poliomyelitis and invasive diseases caused by *Haemophilus influenzae* type b for 3 dose regimen (6, 10 and 14 weeks) for primary vaccination, and a booster dose at the age of 12 to 24 months.

4.2 Posology and method of administration

Posology

Primary vaccination:

For active immunisation of infants, it is recommended that 3 doses of 0,5 mL to be administered with an interval of at least four weeks between doses starting at six weeks of age.

In countries, where peri-natal transmission of hepatitis B virus (HBV) is common, the first dose of hepatitis B should be given as soon as possible after birth. In this case, CIHEXA can be used to complete the primary series from 6 weeks of age.

Booster vaccination:

A booster dose of diphtheria, tetanus, pertussis, *Haemophilus influenza* type b and inactivated polio vaccine should be given preferably during the second year of life (≥ 6 months after last primary dose). Booster doses should be given in accordance with the official recommendations.
Booster dose may be provided to children having received primary vaccinations of CIHEXA or any other diphtheria, tetanus and pertussis containing vaccines and poliomyelitis vaccine (OPV and/or IPV).

Method of administration

CIHEXA liquid vaccine vial should be shaken before use to homogenise the suspension. CIHEXA should be administered intramuscularly. The recommended injection sites are generally the antero-lateral aspect of the upper thigh in infants and toddlers.
Do not administer by intravascular, intradermal or subcutaneous injection.
A sterile syringe and sterile needle must be used for the injection.
Any other injection if co-administered with CIHEXA should be given at a different site.

4.3 Contraindications

CIHEXA is contraindicated in:

- Patients with known hypersensitivity to administration of diphtheria, tetanus, *Bordetella pertussis*, hepatitis B, polio or *Haemophilus influenza* type b vaccines or to any of the excipients in CIHEXA (see **section 6.1**).
- Infants who have experienced an encephalopathy of unknown aetiology, occurring within 7 days following previous vaccination with pertussis containing vaccine (whole cell or acellular pertussis vaccines). Pertussis vaccination should be discontinued, and the

vaccination course should be continued with diphtheria-tetanus, hepatitis B, polio and *Haemophilus influenza* type b vaccines.

- Uncontrolled neurologic disorder or uncontrolled epilepsy. Pertussis vaccine should not be administered to individuals with these conditions until the treatment regimen has been established, the condition has stabilised, and the benefit clearly outweighs the risk.

Generally, vaccination must be postponed in cases of acute moderate or severe febrile illness. The presence of a minor infection and/or low-grade fever does not constitute a contraindication.

4.4 Special warnings and precautions for use

As with any vaccine, a protective immune response may not be elicited in all vaccines. CIHEXA will not prevent disease caused by pathogens other than *Corynebacterium diphtheriae*, *Clostridium tetani*, *Bordetella pertussis*, hepatitis B virus, poliovirus or *Haemophilus influenzae* type b. It does not prevent hepatitis caused by other agents different from HBV (such as virus A, C and E) but it is considered effective in preventing hepatitis caused by the delta agent. *Haemophilus influenza* type b vaccine does not protect against disease due to other types of *Haemophilus influenzae* nor against meningitis caused by other organisms. Due to the long incubation period of hepatitis B (up to 6 months or more), cases where prior exposure to hepatitis B virus has taken place, vaccination may not be effective.

Vaccination should be preceded by a review of medical history (previous vaccinations and possible adverse events). In persons who have a history of serious or severe reaction within 48 hours of a previous injection with a vaccine containing similar components, administration of CIHEXA must be carefully considered.

If any of the following events occur in temporal relation to receipt of CIHEXA, the decision to give subsequent doses of vaccine containing the pertussis component should be carefully considered.

- Temperature 40,5 °C or more within 48 hours of a dose unexplained by another cause.
- Collapse or shock-like state (hypnotic-hypo responsive episode) within 48 hours.
- Persistent, inconsolable crying lasting 3 hours or more occurring within 48 hours.
- Convulsions with or without fever occurring within three days.

There may be circumstances, such as a high incidence of pertussis, when the potential benefits outweigh possible risks.

CIHEXA should not be given to children with any coagulation disorder, including thrombocytopenia that would contraindicate intramuscular injection unless the potential benefit clearly outweighs the risk of administration.

Infants and children with a history of convulsions in first-degree family members (i.e., siblings and parents) when administered diphtheria, tetanus and pertussis containing vaccines have an increased risk for neurologic events and permanent neurologic damage when compared with infants without such history. Infants and children with recognised possible or potential underlying neurologic conditions seem to be at enhanced risk for the appearance of manifestation of the underlying neurologic disorder within two or three days following vaccination.

The administration of CIHEXA vaccine to children with proven or suspected underlying neurologic disorders that are not actively evolving must be decided on an individual basis.

As with the use of all vaccines, the vaccinated individual should remain under observation for not less than 30 minutes for possibility of occurrence of immediate or early allergic reactions. Appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic event following the administration of CIHEXA.

Immune deficiency

Individuals infected with the human immune-deficiency virus (HIV), both asymptomatic and symptomatic, should be immunised with combined vaccine according to standard schedules. Immunosuppressed children may not obtain expected immunological response.

4.5 Interaction with other medicines and other forms of interaction

Concomitant use with other vaccines

CIHEXA can be administered concomitantly with a pneumococcal polysaccharide conjugate vaccine, measles, mumps, rubella (MMR) containing vaccines, oral polio vaccine, rotavirus vaccines, a meningococcal conjugate vaccine, as it is unlikely to result in an interference with the immune responses. CIHEXA can be given safely and effectively at the same time as BCG, yellow fever vaccines and vitamin A supplementation.

If co-administration with another vaccine is considered, immunisation should be carried out on separate injection sites. CIHEXA must not be mixed with any other vaccines or other parenterally administered medicinal products.

As with other intramuscular injections, use with caution in patients on anticoagulant therapy, immunosuppressive therapies, including irradiation, antimetabolites, alkylating agents, cytotoxic medicines and corticosteroids (used in greater than physiologic doses) may reduce the immune response to vaccines. Short-term (< 2 weeks) corticosteroid therapy or intra-articular, bursal or tendon injections with corticosteroids should not be immunosuppressive.

Immune interference (blunting) is a class effect of Tdap vaccines, but that this does not have a clinically significant effect on maternal immunization and does not affect the safety and effectiveness of the vaccine.

4.6 Fertility, pregnancy and lactation

CIHEXA is not intended for administration to women of child-bearing age, thus human data on use during pregnancy or lactation are not available.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

Summary of the safety profile

The safety profile presented below is based on data from pivotal clinical trial (SII-wHEXA/IN-02) conducted in India where CIHEXA was administered to 110 toddlers and 884 infants. The majority of the reactions observed following vaccination were of mild to moderate severity and were of short duration.

Tabulated summary of adverse reactions

Adverse events are organised by MedDRA System Organ Class (SOC). Within each SOC, preferred terms are arranged by decreasing frequency and then by decreasing seriousness. Frequencies of occurrence of adverse events are defined as: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1000 to < 1/100); rare (≥ 1/10000 to < 1/1000) and very rare (< 1/10000).

MedDRA system organ class	Frequency	Side effects
Metabolism and nutrition disorders	Very common	Decreased appetite
Nervous system disorders	Very common	Somnolence
Gastrointestinal disorders	Very common	Vomiting
Skin and subcutaneous tissue disorders	Uncommon	Rash
General disorders and administration site conditions	Very common	Injection site erythema
	Very common	Injection site pain
	Very common	Injection site swelling
	Uncommon	Nodule
	Very common	Crying
	Very common	Irritability
	Very common	Pyrexia

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the “6.04 Adverse Drug Reactions Reporting Form”, found online under SAHPRA’s publications: https://www.sahpra.org.za/Publications/Index/8 or to Cipla Medpro (Pty) Ltd. by email: drugsafetysa@cipla.com or telephone: 080 222 6662 (toll free).

4.9 Overdose

No cases of overdose were reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacological classification: A 30.2 Antigens

Pharmacotherapeutic group: Bacterial and viral vaccines combined.

ATC code: J07CA09

Immunogenicity

The immunogenicity of CIHEXA has been evaluated in a pivotal, multicentric, randomised, controlled clinical trial (SII-wHEXA/IN-02). After 3-dose primary vaccination schedule in infants, robust immune response was achieved for all antigens and non-inferiority was demonstrated against licensed vaccine.

The results of these clinical studies are summarised in the table below.

Seroprotection/Seroconversion rates following primary immunisation and booster dose of CIHEXA

The currently available immunogenicity data on preterm and older children is limited.

Antibody (Cut-off)	**Post dose 3 after primary vaccination at 6-10-14 weeks**			**Post booster vaccination during the second year of life**		
	N	**n**	**(%)**	**N**	**n**	**(%)**
Anti-Diphtheria (≥ 0,1 IU/mL)	804	801	99,6	109	108	99,1
Anti-Tetanus (≥ 0,1 IU/mL)	804	804	100,0	109	109	100,0
Anti-Bordetella Pertussis	804	603	75,0	109	103	94,5

(> 24 U/mL)						
Anti-Pertussis Toxin (Seroconversion*)	804	648	80,6	109	84	77,1
Anti-HBsAG (≥ 10 mIU/mL)	804	787	97,9	110	110	100,0
Anti-PRP (≥ 0,15 µg/mL)	804	799	99,4	109	109	100,0
Anti-Polio Type 1 (≥ 8 (1/dilution))	796	795	99,9	110	110	100,0
Anti-Polio Type 2 (≥ 8 (1/dilution))	796	791	99,4	110	108	98,2
Anti-Polio Type 3 (≥ 8 (1/dilution))	796	795	99,9	110	110	100,0

N = Number of available subjects for each of the antigen

n = Number of subjects achieving seroprotection/seroconversion

*In subjects with no quantifiable antibody – below the LLOQ – prior to vaccination, seroconversion was defined as achieving a quantifiable antibody level post-vaccination. In subjects with quantifiable antibody prior to vaccination, seroconversion was defined by a 4-fold-increase in antibody titres from pre- to post-vaccination.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on a conventional study of acute and repeat dose toxicity.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- 0,9 % Sodium chloride
- 2-Phenoxyethanol
- Aluminium content Al^{+++} (as Aluminium phosphate gel)
- Acetic acid for pH-adjustment
- Sodium hydroxide for pH-adjustment

6.2 Incompatibilities

The vaccine is not to be mixed with other vaccines or other parenterally administered drugs.

6.3 Shelf life

Unopened vial – 24 months.

Opened multidose vial – After first opening, the vaccine can be used for up to 28 days, provided it is stored between 2 and 8 °C

6.4 Special precautions for storage

- Store between 2 and 8 °C.
- Do not freeze. Discard vaccine if frozen.
- Before use, the vaccine should be shaken in order to obtain a homogenous pinkish to yellowish turbid liquid.
- Keep the vaccine in the outer carton in order to protect from light.

- Do not use this vaccine after the expiry date which is stated on the carton and label.
- 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.

6.5 Nature and contents of container

CIHEXA is packed in:

- Single dose – 2 mL USP Type-I, clear tubular glass vial with bromobutyl rubber stopper and aluminium flip off seal.

Pack size: 50 labelled vials are packed in one cardboard carton.

- Multi dose – 5 mL USP Type-I, clear tubular glass vial with bromobutyl rubber stopper and aluminium flip off seal.

Pack size: 50 labelled vials are packed in one cardboard carton.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

CIPLA MEDPRO (PTY) LTD.

Building 9

Parc du Cap

Mispel Street

Bellville

7530

Customer Care: 080 222 6662

8. REGISTRATION NUMBER

59/30.2/0479

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

First authorisation: 30 September 2025.

Latest renewal: Not applicable.

10. DATE OF REVISION OF THE TEXT

Not applicable