▼This medicinal product is subject to additional monitoring in Australia. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse events at www.tga.gov.au/reporting-problems.

# AUSTRALIAN PRODUCT INFORMATION - VAXELIS

**(Diphtheria, tetanus, pertussis (acellular components), hepatitis B, poliovirus (inactivated), and *Haemophilus influenzae* type b conjugate vaccine**

## 1 NAME OF THE MEDICINE

Vaxelis

Diphtheria, tetanus, pertussis (acellular, component), hepatitis B, poliovirus (inactivated), and *Haemophilus influenzae* type b conjugate vaccine

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One dose (0.5 mL) contains:

| | |
|---|---|
| Diphtheria Toxoid[1] | not less than 20 IU[6] |
| Tetanus Toxoid[1] | not less than 40 IU[6] |
| *Bordetella pertussis antigens*[1] | |
| Pertussis Toxoid (PT) | 20 micrograms |
| Filamentous Haemagglutinin (FHA) | 20 micrograms |
| Pertactin (PRN) | 3 micrograms |
| Fimbriae Types 2 and 3 (FIM) | 5 micrograms |
| Hepatitis B surface antigen[2,3] | 10 micrograms |
| Poliovirus (Inactivated)[4] | |
| Type 1 (Mahoney) | 40 D antigen units[5] |
| Type 2 (MEF-1) | 8 D antigen units[5] |
| Type 3 (Saukett) | 32 D antigen units[5] |
| *Haemophilus influenzae* type b polysaccharide | |
| (Polyribosylribitol Phosphate) | 3 micrograms |
| Conjugated to meningococcal protein[2] | 50 micrograms |

[1] adsorbed on aluminium phosphate (0.17 mg $Al^{3+}$)
[2] adsorbed on amorphous aluminium hydroxyphosphate sulfate (0.15 mg $Al^{3+}$)
[3] produced in yeast (*Saccharomyces cerevisiae*) cells by recombinant DNA technology
[4] produced in Vero cells
[5] or equivalent antigenic quantity determined by a suitable immunochemical method
[6] or equivalent activity determined by an immunogenicity evaluation.

The vaccine may contain traces of glutaraldehyde, formaldehyde, neomycin, streptomycin, polymyxin B, and bovine serum albumin which are used during the manufacturing process (see section 4.3 Contraindications).

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

# 3 PHARMACEUTICAL FORM

Suspension for injection.

Uniform, cloudy, white to off-white suspension.

# 4 CLINICAL PARTICULARS

## 4.1 THERAPEUTIC INDICATIONS

Vaxelis (DTPa5-HepB-IPV-Hib) is indicated for primary and booster vaccination in infants and toddlers from the age of 6 weeks, against diphtheria, tetanus, pertussis, hepatitis B (Hep B), poliomyelitis and invasive diseases caused by *Haemophilus influenzae* type b (Hib).

The use of Vaxelis should be in accordance with official recommendations.

## 4.2 DOSE AND METHOD OF ADMINISTRATION

Primary vaccination:

The primary vaccination schedule consists of 2 or 3 doses, with an interval of at least 1 month between doses, and may be given from 6 weeks of age, in accordance with the official recommendations.

Where a dose of hepatitis B vaccine is given at birth, Vaxelis can be used for supplementary doses of hepatitis B vaccine from the age of 6 weeks. If a second dose of hepatitis B vaccine is required before this age, monovalent hepatitis B vaccine should be used. Vaxelis can be used for a mixed hexavalent/pentavalent/hexavalent combined vaccine immunisation schedule.

Booster vaccination:

After a 3-dose primary series vaccination with Vaxelis, a booster dose may be given. When giving a booster dose, this should be at least 6 months after the last priming dose. After a 2-dose primary series vaccination with Vaxelis, a booster dose should be given at least 6 months after the last priming dose.

Booster doses should be given in accordance with the official recommendations.

### *Method of administration*

Vaxelis should only be administered by intramuscular (IM) injection. The recommended injection sites are the anterolateral area of the thigh (preferred site for infants under one year of age) or the deltoid muscle of the upper arm.

Vaxelis is for single use only and must not be used in more than one individual. Discard any remaining unused contents.

Instructions for use:

Prior to administration, the pre-filled syringe should be shaken gently in order to obtain a homogeneous, whitish, cloudy suspension.

The suspension should be visually inspected, prior to administration, for foreign particulate matter and/or variation of physical appearance. If either is observed, discard the pre-filled syringe (see section 6.6 Special precautions for disposal).

The needle must be fitted firmly on to the pre-filled syringe, rotating it by a one quarter turn.

## 4.3 CONTRAINDICATIONS

### *Hypersensitivity*

History of an anaphylactic reaction after a previous administration of Vaxelis or a vaccine containing any of the same components, constituents or residues (see section 2 Qualitative and quantitative composition).

### *Neurological Disorders*

Encephalopathy of unknown aetiology, occurring within 7 days following prior vaccination with a pertussis containing vaccine. In these circumstances, pertussis vaccination should be discontinued, and the vaccination course should be continued with diphtheria, tetanus, hepatitis B, poliomyelitis, and Hib vaccines.

Uncontrolled neurologic disorder or uncontrolled epilepsy: pertussis vaccination should not be administered until treatment for the condition has been established, the condition has stabilised, and the benefit clearly outweighs the risk.

## 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Do not administer by intravascular, intradermal or subcutaneous injection.

### *Protection*

Vaxelis will not prevent disease caused by pathogens other than *Corynebacterium diphtheriae*, *Clostridium tetani*, *Bordetella pertussis*, hepatitis B virus, poliovirus or *Haemophilus influenzae* type b. However, it can be expected that hepatitis D will be prevented by immunisation as hepatitis D (caused by the delta agent) does not occur in the absence of hepatitis B infection.

Vaxelis will not protect against hepatitis infection caused by other agents such as hepatitis A, hepatitis C and hepatitis E or by other liver pathogens.

Because of the long incubation period of hepatitis B, it is possible for hepatitis B infection to be present at the time of vaccination. The vaccine may not prevent hepatitis B infection in such cases.

Vaxelis does not protect against disease caused by *Haemophilus influenzae* other than type b or by other microorganisms that cause invasive disease such as meningitis or sepsis, including *N. meningitidis*.

As with any vaccine, a protective immune response may not be elicited in all vaccinees.

***Prior to immunisation***

Vaccination should be preceded by a review of the individual's medical history (in particular, previous vaccinations and possible adverse reactions).

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 4.3 Contraindications).

***Acute or febrile disease***

As with other vaccines, administration of Vaxelis should be postponed in children suffering from moderate to severe acute disease, with or without fever. The presence of a minor illness and /or low- grade fever does not constitute a contraindication.

***Prior history of severe adverse events following pertussis vaccination***

If any of the following events have occurred after administration of a pertussis-containing vaccine, the decision to administer further doses of a pertussis-containing vaccine should be carefully considered:

- Temperature of ≥40°C within 48 hours, not attributable to another identifiable cause
- Collapse or shock-like state (hypotonic-hyporesponsive episode [HHE]) within 48 hours of vaccination

Persistent inconsolable crying lasting ≥3 hours, occurring within 48 hours of vaccination where no other cause can be identified

- Convulsions with or without fever, occurring within 3 days of vaccination.

There may be some circumstances, such as high incidence of pertussis, when the potential benefits outweigh possible risks particularly since these events are not associated with permanent sequelae.

***Neurological adverse events***

If Guillain-Barré syndrome has occurred within 6 weeks of receipt of prior vaccine containing tetanus toxoid, the decision to give any vaccine containing tetanus toxoid, including Vaxelis, 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 Vaxelis. Individuals with a history of febrile convulsions should be closely followed up as febrile convulsions may occur within 2 to 3 days post vaccination.

***Coadministration***

Data from a clinical study indicate that, when Vaxelis is co-administered with pneumococcal conjugate vaccine (PCV13), the rate of fever is higher following the booster dose in the second year of life compared to the primary series. Almost all fevers were mild or moderate (<39.5°C) and transient (duration of ≤2 days) (see section 4.8 Adverse effects).

### *Premature infants*

Limited data from 111 pre-term newborn infants in clinical trials indicate that Vaxelis can be given to premature infants. The immune responses to Vaxelis in these infants were generally similar to those of the overall study population. However, a lower immune response may be observed, and the level of clinical protection is unknown.

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 should not be withheld or delayed.

### *Genetic Polymorphism*

Immune responses to the vaccine have not been studied in the context of genetic polymorphism.

### *Immunocompromised children*

The immunogenicity of the vaccine may be reduced by immunosuppressive treatment or immunodeficiency. It is recommended to postpone vaccination until the end of such treatment or disease. Nevertheless, vaccination of individuals with chronic immunodeficiency such as HIV infection is recommended even if the antibody response may be limited. No data currently exist on use of Vaxelis in immunocompromised children.

### *Blood disorders*

As with all injectable vaccines, the vaccine must be administered with caution to individuals with thrombocytopenia or a bleeding disorder since bleeding may occur following an intramuscular administration.

### *Use in the elderly*

Not applicable.

### *Paediatric use*

The safety and efficacy of Vaxelis in infants less than 6 weeks of age have not been established. No data are available.

### *Effects on laboratory tests*

Since the Hib capsular polysaccharide antigen is excreted in the urine, a false positive urine test can be observed using sensitive tests, for at least 30 days following vaccination. Other tests should be performed in order to confirm Hib infection during this period.

## 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Vaxelis may be administered simultaneously with pneumococcal polysaccharide conjugate vaccines, rotavirus vaccines, measles, mumps, rubella (MMR) and varicella containing vaccines and meningococcal C conjugate vaccines.

**Concomitant administration with PCV 13**

Data from a clinical study indicate that, when Vaxelis is co-administered with pneumococcal conjugate vaccine (PCV13), the rate of fever is higher following the booster dose in the second year of life compared to the primary series. Almost all fevers were mild or moderate (<39.5°C) and transient (duration of ≤2 days) (see section 4.8 Adverse effects).

Co-administration of Vaxelis with other injectable vaccines must be carried out at separate injection sites and, preferably, separate limbs.

Vaxelis should not be mixed with any other vaccine or other parenterally administered medicinal products.

Immunosuppressive therapy may interfere with the development of expected immune response (see section 4.4 Special warnings and precautions for use).

## 4.6 FERTILITY, PREGNANCY AND LACTATION

### *Effects on fertility*

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

### *Use in pregnancy (Category B2)*

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

### *Use in 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

Although no such studies have been performed, it is expected that Vaxelis would have no or negligible influence on the ability to use bicycles and other such machines.

## 4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

### *Summary of the safety profile*

The data from 6 clinical trials conducted in several countries and using various immunisation schedules were pooled. In these studies, Vaxelis was administered as a primary series vaccine (N >5200) and as a booster dose (N >1500). The adverse reactions occurring after vaccination are summarised in Table 1 below.

The most frequently reported adverse reactions after Vaxelis administration were irritability, crying, somnolence, injection site reactions (pain, erythema, swelling), pyrexia (≥38°C), decreased appetite, and vomiting.

The rates of solicited adverse reactions from the 4 pivotal Ph 3 studies are provided in Table 2.

The safety of Vaxelis in children over 15 months of age has not been studied in clinical trials.

In a clinical study where Vaxelis was administered concomitantly with Prevenar 13 (PCV13) as a booster dose of both vaccines, fever ≥38.0°C was reported in 52.5% of children, compared to 33.1% to 40.7% of children during the primary series. Fever ≥39.5°C was observed in 3.7% of children (post- booster) and 0.2% to 0.8% of children (post-primary) receiving Vaxelis with PCV13 (see sections 4.4 Special warnings and precautions for use and 4.5 Interactions with other medicines). Almost all fevers after primary and booster doses were mild or moderate (<39.5°C) and transient (duration of ≤2 days).

### *Tabulated list of adverse reactions*

The following convention has been used for the classification of adverse reactions:
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)
Not known (cannot be estimated from the available data)

**Table 1 - List of Adverse Reactions**

| System Organ Class | Frequency | Adverse Reactions |
|---|---|---|
| Infections and infestations | Uncommon | Rhinitis |
| Blood and lymphatic system disorders | Uncommon | Lymphadenopathy |
| Metabolism and nutrition disorders | Very Common | Decreased appetite |
| | Uncommon | Increased appetite |
| Psychiatric disorders | Uncommon | Sleep disorders including insomnia, restlessness |
| Nervous system disorders | Very Common | Somnolence |
| | Uncommon | Hypotonia |
| Vascular disorders | Uncommon | Pallor |
| Respiratory, thoracic and mediastinal disorders | Uncommon | Cough |
| Gastrointestinal disorders | Very Common | Vomiting |
| | Common | Diarrhoea |
| | Uncommon | Abdominal pain |
| Skin and subcutaneous tissue disorders | Uncommon | Rash, hyperhidrosis |
| General disorders and administration site conditions | Very Common | Crying, irritability |
| | | Injection site erythema, injection site pain, injection site swelling |
| | | Pyrexia |

| System Organ Class | Frequency | Adverse Reactions |
|---|---|---|
| | Common | Injection site bruising, injection site induration, injection site nodule |
| | Uncommon | Injection site rash, injection site warmth, fatigue |

**Table 2: Percentage of infants with solicited adverse reactions occurring within 5 days post any vaccination with Vaxelis compared with Control Vaccines**

| | Study 008 2, 4 and 11–12 months | | Study 007 2, 3, 4 and 12 months | | Study 006 2, 4 and 6 months | | Study 005 2, 4 and 6 months | |
|---|---|---|---|---|---|---|---|---|
| | Vaxelis | Control[1] | Vaxelis | Control[1] | Vaxelis | Control[2] | Vaxelis | Control[2] |
| **Injection Site Adverse Reactions** | | | | | | | | |
| Pain | 73.4 | 70.0 | 73.6 | 71.8 | 70.0 | 72.0 | 73.4 | 71.8 |
| Erythema | 68.6 | 60.4 | 69.0 | 64.2 | 44.6 | 40.8 | 48.8 | 42.2 |
| Swelling | 56.8 | 49.3 | 56.9 | 52.9 | 34.5 | 34.5 | 40.1 | 34.8 |
| **Systemic Adverse Reactions** | | | | | | | | |
| Irritability | 91.6 | 89.4 | 87.9 | 85.7 | 80.7 | 79.8 | 83.1 | 81.8 |
| Crying | 89.3 | 87.1 | 85.4 | 87.9 | 74.8 | 72.5 | 74.8 | 72.3 |
| Somnolence | 86.1 | 80.3 | 76.9 | 80.1 | 73.2 | 73.3 | 74.1 | 71.6 |
| Pyrexia ≥38°C | 73.8 | 67.4 | 71.5 | 73.1 | 47.1 | 33.2 | 47.4 | 34.4 |
| Decreased appetite | 65.8 | 62.2 | 63.9 | 67.0 | 48.5 | 47.4 | 48.9 | 43.3 |
| Vomiting | 32.8 | 31.0 | 31.8 | 31.0 | 26.7 | 24.9 | 25.7 | 21.5 |

[1] DTPa-HepB-IPV-Hib vaccine
[2] DTPa-IPV-Hib vaccine and HepB vaccine

### *Post-Marketing Surveillance*

The following adverse events have been reported during post-marketing use. Because these events were reported from a population of uncertain size, it is generally not possible to reliably estimate their frequency or to establish, a causal relationship to the vaccine.

| System Organ Class | Frequency | Adverse Event |
|---|---|---|
| Immune system disorders | Not known | Hypersensitivity (such as rash, urticaria, dyspnea, erythema multiforme), anaphylactic reaction (such as urticaria, edema, face edema, shock). |
| Nervous system disorders | Not known | Hypotonic-hyporesponsive episode (HHE), convulsions with or without fever (see section 4.4 Special warnings and precautions for use) |
| General disorders and administration site conditions | Not known | Extensive swelling of the vaccinated limb (including swelling that involves one or both adjacent joints). |

### *Description of selected adverse reactions*

*General disorders and administration site conditions*

Extensive swelling of the vaccinated limb from the injection site beyond one or both joints, has been reported in children. These reactions start within 24 to 72 hours after vaccination, may be associated with erythema, warmth, tenderness or pain at the injection site and resolve spontaneously within 3 to 5 days. The risk appears to be dependent on the number of prior doses of acellular pertussis containing vaccine, with a greater risk following the 4$^{th}$ and 5$^{th}$ doses.

### *Premature infants*

Apnoea in very premature infants (≤28 weeks of gestation) (see section 4.4 Special warnings and precautions for use).

### *Reporting suspected adverse effects*

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems (Australia) or https://nzphvc.otago.ac.nz/reporting/ (New Zealand).

## 4.9 OVERDOSE

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia) or the National Poisons Centre on 0800 POISON or 0800 764 766 (New Zealand).

# 5 PHARMACOLOGICAL PROPERTIES

## 5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: Vaccines, Bacterial and viral vaccines combined, ATC code: J07CA09

### *Mechanism of action*

Vaxelis induces the production of antibodies against diphtheria, tetanus, pertussis, hepatitis B, poliovirus and invasive diseases caused by *Haemophilus influenzae* type b.

### *Clinical trials*

The immunogenicity of Vaxelis was evaluated in 4 pivotal Ph 3 clinical studies in which infants 43–99 days of age at enrollment received at least 1 dose of Vaxelis. Clinical study comparators were either pentavalent (DTPa-IPV-Hib) and HepB or hexavalent (DTPa-HepB-IPV-Hib) vaccines. See Table 3

**Table 3: Vaxelis pivotal study designs for immunogenicity**

| Study | Primary infant series | | | Toddler dose | | |
|---|---|---|---|---|---|---|
| | months | Test group | Control group | months | Test group | Control group |

| | | | | | | |
|---|---|---|---|---|---|---|
| 008 | 2, 4 | Vaxelis | DTPa-HepB-IPV-Hib‡ | 11–12 | Vaxelis | DTPa-HepB-IPV-Hib‡ |
| 007 | 2, 3, 4 | Vaxelis | DTPa-HepB-IPV-Hib‡ | 12 | Vaxelis | DTPa-HepB-IPV-Hib‡ |
| 006 | 2, 4, 6 | Vaxelis | DTPa-IPV-Hibł,§ | 15 | DTPa-IPV-Hib | DTPa-IPV-Hib§ |
| 005 | 2, 4, 6 | Vaxelis | DTPa-IPV-Hibł,§ | 15 | DTPa#,1 | DTPa*,2 |

łplus Monovalent Hep B vaccine at 2, 6 months

#,1plus Haemophilus b Conjugate vaccine (Meningococcal protein conjugate)

*,2plus Haemophilus b Conjugate Vaccine (Tetanus Toxoid Conjugate).

§Diphtheria and tetanus toxoids and acellular pertussis Adsorbed, inactivated poliovirus and Haemophilus b Conjugate (Tetanus Toxoid Conjugate) Vaccine.

‡Diphtheria, tetanus, pertussis (acellular, component), hepatitis B (recombinant deoxyribonucleic acid), inactivated poliovirus and Haemophilus type b conjugate (Tetanus toxoid conjugate) Vaccine.

## Immunogenicity after primary series and booster doses

The Vaxelis primary vaccination schedules used in clinical studies were: 2, 4 months of age without hepatitis B vaccination at birth; 2, 3, 4 months of age without hepatitis B vaccination at birth; and 2, 4, 6 months of age with and without hepatitis B vaccination at birth. The Vaxelis booster dose in clinical studies was given at 11–12 months of age after a 2-dose primary series and at 12 months of age after a 3-dose primary series (2, 3, 4 months). In two studies, a non-Vaxelis booster dose was given at 15 months of age after a 3 dose primary series (2, 4, 6 months). Results obtained for each component of the vaccine are summarised in Table 4 and Table 5.

**Table 4 - Seroprotection/vaccine response rates one month after the primary vaccination series**

| Antibody Thresholds | | Post-Two doses | Post-Three doses | |
|---|---|---|---|---|
| | | 2, 4 months | 2, 3, 4 months | 2, 4, 6 months* |
| | | N = 319-609<br>% | N = 498-550<br>% | N = 2455-2696<br>% |
| Anti-diphtheria (≥ 0.01 IU/mL) | | 98.3 | 99.8 | 99.8 |
| Anti-tetanus (≥ 0.01 IU/mL) | | 100.0 | 100.0 | 100.0 |
| Anti-PT (vaccine response)[a] | | 98.1 | 99.4 | 98.9 |
| Anti-FHA (vaccine response)[a] | | 89.0 | 89.0 | 88.1 |
| Anti-PRN (vaccine response)[a] | | 80.3 | 86.7 | 84.0 |
| Anti-FIM (vaccine response)[a] | | 93.3 | 97.2 | 90.0 |
| Anti-Polio type 1 (≥ 1:8 dilution) | | 93.8 | 100.0 | 100.0 |
| Anti-Polio type 2 (≥ 1:8 dilution) | | 98.0 | 99.8 | 100.0 |
| Anti-Polio type 3 (≥ 1:8 dilution) | | 92.9 | 100.0 | 100.0 |
| Anti-HBs Ag (≥ | With hepatitis B vaccination at birth | / | / | 99.8 |

| | | | | |
|---|---|---|---|---|
| 10 mIU/mL) | Without hepatitis B vaccination at birth | 98.1 | 97.8 | 97.8[b] |
| Anti-PRP (≥ 0.15 µg/mL) | | 96.6 | 98.4 | 98.1 |

[a]Vaccine response: If pre-dose 1 antibody concentration < lower limit of quantification (LLOQ), then the post-vaccination series antibody concentration was ≥ LLOQ; if pre-dose 1 antibody concentration ≥ LLOQ, then the post-vaccination series antibody concentration was ≥ pre-dose 1 levels. LLOQ = 4 EU/mL are for anti-PT, anti-PRN and anti-FIM; and LLOQ = 3 EU/mL for anti-FHA
[b]N=89 subjects from a separate study
*Study 005 and 006 combined data

**Table 5 - Seroprotection/vaccine response rates pre-booster and one month after booster vaccination**

| Antibody Thresholds | 2, 4 and 11-12 month study | | 2, 3, 4 and 12 month study | | 2, 4, 6 and 15 month study | | | |
|---|---|---|---|---|---|---|---|---|
| | Study 008 | | Study 007 | | Study 006 | | Study 005 | |
| | Pre-booster | One month after booster | Pre-booster | One month after booster | Pre-booster | One month after booster | Pre-booster | One month after booster |
| | N = 593-614 % | N = 377-591 % | N = 542-555 % | N = 439-551 % | N= 1598–1673 % | N= 1577–1734 % | N= 691–704 % | N = 687–712 % |
| Anti-diphtheria (≥ 0.1 IU/mL) | ND | 98.6 | ND | 99.8 | ND | 99.9 | ND | 100.0 |
| Anti-tetanus (≥ 0.1 IU/mL) | ND | 99.8 | ND | 100.0 | ND | 100.0 | ND | 100.0 |
| Anti-PT (vaccine response)[a] | 79.4 | 99.1 | ND | 99.8 | 22.8 | 98.5 | 22.9 | 99.3 |
| Anti-FHA (vaccine response)[a] | 58.8 | 97.4 | ND | 97.2 | 21.7 | 95.3 | 22.5 | 94.4 |
| Anti-PRN (vaccine response)[a] | 53.9 | 96.9 | ND | 99.3 | 19.3 | 92.2 | 17.5 | 93.0 |
| Anti-FIM (vaccine response)[a] | 78.1 | 98.3 | ND | 99.6 | 59.2 | 93.0 | 60.6 | 97.3 |
| Anti-Polio type 1 (≥ 1:8 dilution) | ND | 99.3 | ND | 99.8 | ND | 100.0 | ND | 99.4 |
| Anti-Polio type 2 (≥ 1:8 dilution) | ND | 99.8 | ND | 100.0 | ND | 100.0 | ND | 99.6 |
| Anti-Polio type 3 (≥ 1:8 dilution) | ND | 99.5 | ND | 100.0 | ND | 99.9 | ND | 97.7 |
| Anti-HBs Ag (≥ 10 mIU/mL)[b] | 89.4 | 98.1 | 91.2 | 99.6 | 94.7 | 93.8 | 93.6 | 92.0 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Anti-PRP | (≥ 0.15 µg/mL) | 91.4 | 99.6 | 94.7 | 99.5 | 89.6 | 99.6 | 93.2 | 99.6 |
| | (≥ 1.0 µg/mL) | 50.1 | 89.9 | 57.8 | 95.0 | 43.9 | 100.0 | 42.1 | 95.3 |

[a]Vaccine response: If pre-dose 1 antibody concentration < LLOQ, then post-booster antibody concentration should be ≥ LLOQ; If pre-dose 1 antibody concentration ≥ LLOQ, then the post-booster antibody concentration should be ≥ pre-dose 1 levels. LLOQ = 4 EU/mL are for anti-PT, anti-PRN and anti-FIM; and LLOQ = 3 EU/mL for anti-FHA
[b]Did not receive hepatitis B vaccine at birth
ND = Not Determined

Regarding PT and FIM, similar response rates and higher GMCs were observed both post-primary and post-booster in comparison to control vaccine. Lower FHA, PRN, IPV1 and IPV3 immune responses were observed after a 2-dose primary schedule (2, 4 months), although the clinical relevance of these data remains uncertain. Pertussis response rates were similar to the control vaccine for all pertussis antigens after the booster dose.

The immunogenicity of Vaxelis administered to children over 15 months of age has not been studied in clinical trials.

**Persistence of the immune response**

Hepatitis B immune memory

The persistence of immune responses was evaluated in children up to 8 years after primary vaccination with Vaxelis. The proportions of these children with anti-HBsAg ≥ 10 mIU/mL after having received Vaxelis either at 2, 4, and 11-12 months or at 2, 3, 4, and 12 months of age, respectively were:

- 65.8% (119 of 181) and 70.2% (134 of 191), respectively, at 4–5 years of age
- 40.9% (38 of 93) and 49.1% (55 of 112), respectively, at 8–9 years of age

A hepatitis B vaccine challenge dose was given to children 8–9 years of age. Approximately 1 month after this challenge dose, the proportions with anti-HBsAg ≥ 10 mIU/mL were 100% (93 of 93) and 99.1% (108 of 109), respectively. These data demonstrate an anamnestic response after a challenge dose, indicating the persistence of hepatitis B immune memory in persons who previously received Vaxelis.

Persistence of antibodies to pertussis antigens

The persistence of pertussis antibodies was measured in children 4 or 5 years of age who had received Vaxelis at 2, 4 and 11-12 months of age. The percentages of these children with anti-pertussis antibodies above ≥ the lower limit of quantitation were: anti-PT 58.4%, anti-FHA 80.9%, anti-PRN 66.1% and anti-FIM 94. 4%.

## 5.2 PHARMACOKINETIC PROPERTIES

No pharmacokinetic studies have been performed.

## 5.3 PRECLINICAL SAFETY DATA

### *Genotoxicity*

Vaxelis has not been evaluated for genotoxic potential.

### *Carcinogenicity*

Vaxelis has not been evaluated for carcinogenic potential.

# 6 PHARMACEUTICAL PARTICULARS

## 6.1 LIST OF EXCIPIENTS

Dibasic sodium phosphate and monobasic sodium phosphate

Water for injections

For adjuvants, see section 2 Qualitative and quantitative composition.

## 6.2 INCOMPATIBILITIES

In the absence of compatibility studies, this vaccine must not be mixed with other vaccines or medicinal products.

## 6.3 SHELF LIFE

48 months

## 6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store in a refrigerator (2°C – 8°C).
Do not freeze.
Keep the pre-filled syringe in the outer carton in order to protect from light.
Stability data indicate that the vaccine is stable at temperatures up to 25°C for 150 hours. At the end of this period Vaxelis should be used or discarded. These data are intended to guide healthcare professionals in case of a temporary temperature excursion only.

## 6.5 NATURE AND CONTENTS OF CONTAINER

0.5 mL suspension in pre-filled syringe with a Luer-lock connection (type I glass), plunger stopper (butyl) and tip cap (butyl), without needle – pack size of 1 or 10.

The syringe plunger stopper and syringe tip cap are not made with natural rubber latex.

Not all pack sizes may be marketed.

## 6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

# 7 MEDICINE SCHEDULE (POISONS STANDARD)

Schedule 4 – Prescription medicine

# 8 SPONSOR

Maxx Pharma Pty Ltd
Level 20, 181 William Street
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# 9 DATE OF FIRST APPROVAL

23 March 2022

# 10 DATE OF REVISION

11 July 2024

### SUMMARY TABLE OF CHANGES

| Section Changed | Summary of new information |
|---|---|
| **4.1, 5.1** | Editorial change |
| **4.2, 6.4, 6.5** | Removal of vial presentation |
| **8** | Addition of distributor |