PACKAGE INSERT

(ENGLISH)

Pertagen®

(Recombinant acellular pertussis vaccine)

PACKAGE INSERT

Pertagen®

DESCRIPTION

Pertagen® is a recombinant acellular pertussis vaccine. **Pertagen®** is a sterile, whitish, turbid and uniform suspension. This vaccine contains purified *Bordetella pertussis* antigens (rPT and FHA) which are adsorbed on aluminum hydroxide. rPT (recombinant Pertussis Toxin) is a genetically-detoxified PT obtained by recombinant DNA technology. **Pertagen®** meets the World Health Organisation requirements for the manufacture of biological substances and acellular pertussis vaccines.

COMPOSITION

Each single dose (0.5 mL) contains:

Purified *Bordetella pertussis* antigens

Recombinant Pertussis Toxin (rPT)	5 µg
Filamentous Haemagglutinin (FHA)	5 µg

Excipients: aluminum hydroxide, sodium chloride, water for injection.

Formaldehyde may be present as in trace amounts as a manufacturing process residual.

INDICATION

Pertagen® is indicated for active booster immunization against pertussis in individuals from the age of 11 years onwards. **Pertagen®** may be considered as an alternative to combined tetanus, diphtheria and acellular pertussis vaccines in persons having received multiple and frequent tetanus and diphtheria vaccine doses including persons with known hypersensitivity to tetanus (Arthus-type hypersensitivity reaction) or diphtheria vaccines.

POSOLOGY

A single 0.5 mL dose of **Pertagen®** is recommended. **Pertagen®** should be given following the current local recommendation for booster vaccination against pertussis.

In accordance with 2019 WHO recommendations for routine immunization of pertussis-containing vaccine, the use of **Pertagen®** may be considered in the second or third trimester and preferably at least 15 days before the end of pregnancy. See **PREGNANCY AND LACTATION** section.

MODE OF ADMINISTRATION

Shake the syringe well to obtain a uniform, cloudy and white suspension. Do not use if resuspension does not occur after vigorous shaking.

Pertagen® should be administered by deep intramuscular injection, preferably in the deltoid region. Before injection, the skin over the site of injection should be cleaned with a suitable germicide. Open the needle cap of the pre-filled syringe, administer the total volume of 0.5 mL intramuscularly (IM).

CONTRAINDICATION

Pertagen® should not be administered to individuals having shown signs of hypersensitivity or life-threatening reaction following administration of pertussis vaccines or to any components of the vaccine.

Hypersensitivity to diphtheria and tetanus vaccines are not contraindication to the use of **Pertagen®**.

Pertagen® should not be administered to individuals having experienced any encephalopathy with unknown aetiology such as coma, prolonged seizures, or decreased level of consciousness within 7 days following previous vaccination with any whooping cough vaccine.

Pertagen® should not be administered to individuals with progressive or unstable neurological disorders, uncontrolled epilepsy or progressive encephalopathy.

WARNING AND PRECAUTION

It is good clinical practice that vaccination should be preceded by a review of the medical history (especially with regard to previous vaccination and possible occurrence of undesirable events) and a clinical examination in compliance with local requirements. As with all injectable vaccines, appropriate medical care should be readily available in case of a rare anaphylactic reaction after vaccination.

- The vaccine should not be administered intravascularly.
- Fractional doses (< 0.5 mL) should not be given.

As with other vaccines, administration of **Pertagen®** to subjects suffering from acute severe febrile illness should be postponed. **Pertagen®** should be administered with precautionary measures to subjects who had any of the following adverse events within 48 hours after a previous immunization with any whooping cough vaccines: high temperature (≥ 40°C) without any identifiable cause, convulsions and collapse or shock-like state.

Pertagen® should be administered with caution to the recipient with any bleeding disorders, thrombocytopenia or anticoagulant therapy because bleeding at injection site may occur after intramuscular injection.

In the case of immunosuppressive treatment or immunodeficiency, the immune response to the vaccine may be diminished. Vaccination should be postponed until the end of treatment or resolution of disease. Nevertheless, in the case of chronic immunodeficiency, including HIV-infected persons, vaccination is recommended even if the response may be limited.

INTERACTIONS WITH OTHER DRUGS

Interaction studies with other medicinal products or vaccines have not been performed. However, since **Pertagen®** is an inactivated vaccine, administration of **Pertagen®** concomitantly with other inactivated vaccines or immunoglobulins is unlikely to cause any interference with the immune response.

When considered necessary, **Pertagen®** can be administered simultaneously with other inactivated vaccines or immunoglobulins at separate site of injections.

Immunosuppressive treatment may interfere the development of expected immune response.

PREGNANCY AND LACTATION

Pregnancy

Maternal immunization can protect newborns and young infants who bear the brunt pertussis mortality (WHO Immunological Basis for Immunization Series, Module 4 Pertussis, 2017). In the USA, moderate to severe local reactions have been associated with high levels of tetanus and diphtheria antitoxin when tetanus toxoid was administered with a reduced amount of diphtheria toxoid. However, because of the potential benefits of maternal pertussis immunization and the lack of monovalent acellular pertussis vaccine in the USA, the Advisory Committee on Immunization Practices (ACIP) recommends that pregnant women receive Tdap boosters during each pregnancy (WHO Global Advisory Committee on Vaccine Safety, 2014).

The previous WHO consideration supports the potential use of **Pertagen®**, a monovalent acellular pertussis vaccine, for maternal pertussis immunization.

In accordance with 2019 WHO recommendations for routine immunization of pertussis-containing vaccine, the use of **Pertagen®** may be considered in the second or third trimester and preferably at least 15 days before the end of pregnancy.

Safety data from active post-marketing surveillance (including a prospective observational study) where 964 pregnant women were exposed to **Pertagen®** (monovalent aP vaccine) or to the aP vaccine of **Pertagen®** combined with tetanus toxoid and reduced diphtheria toxoid (TdaP vaccine, **Boostagen®**) in the second or third trimester of pregnancy have shown no vaccine related adverse effect on pregnancy or the health of newborns.

No adverse effects on pregnancy, parturition, lactation or prenatal and postnatal development were observed in one animal toxicity study evaluating **Pertagen®** antigens combined to tetanus and diphtheria toxoids. Data in humans from randomized controlled trials on the use of **Boostagen®** (TdaP vaccine containing **Pertagen®** antigens combined to tetanus and diphtheria toxoids) during the second or third trimester of pregnancy are not yet available. While vaccination with **Pertagen®** is not expected to be associated with any increased risk to the foetus as the vaccine is inactivated, **Pertagen®** should only be used during pregnancy when the possible advantages outweigh the possible risks for the foetus. .

Lactation

The effect of **Pertagen®** during lactation has not been assessed in humans. While no risk to the breastfed infant should be expected as the vaccine is inactivated, **Pertagen®** should only be used during breastfeeding when the possible advantages of vaccination outweigh the potential risks.

UNDESIRABLE EFFECTS

Summary of the safety profile

The safety profile presented below is based on data from a clinical trial where **Pertagen®** was administered to 150 adolescents between 12 and 17 years of age. Within 7 days after vaccination, the most common events occurring were local injection site pain and systemic

reactions (headache, fatigue, myalgia, malaise and arthralgia). Frequency, severity and duration of adverse reactions were similar in subjects vaccinated either with **Pertagen®** or with a licensed Tdap vaccine. These signs and symptoms were mostly mild and moderate in intensity and resolved without sequelae.

Tabulated summary of adverse reactions

Adverse reactions are listed according to the following frequency:

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)

Adolescents 12 – 17 years of age, Adverse Reactions Reported

Frequency	Adverse Reaction/Event	System Organ Class
Very common: ≥1/10	Pain at injection site, malaise, fatigue	General disorders and administration site conditions
	Headache	Nervous system disorders
	Myalgia, arthralgia	Musculoskeletal and connective tissue disorders
Common: ≥1/100 to <1/10	Redness and induration at injection site, chills, fever (≥37.5ºC)	General disorders and administration site conditions
	Vomiting	Gastrointestinal disorders
Uncommon: ≥1/1000 to <1/100	Injection site swelling	General disorders and administration site conditions
	Lymphadenitis	Blood and lymphatic system disorders
	Pain in extremity	Musculoskeletal and connective tissue disorders
	Eye pain	Eye disorders

In another clinical trial, a formulation of recombinant acellular pertussis vaccine containing PRN (Pertactin antigen) in addition to the **Pertagen®** antigens (rPT and FHA) was tested in 20 healthy adult subjects aged 18 – 35 years. Subjects vaccinated with this vaccine had similar frequency of adverse events following 7 days after vaccination to subjects vaccinated with a licensed Tdap vaccine.

Adults 18 – 35 years of age, Adverse Reactions Reported

Frequency	Adverse Reaction/Event	System Organ Class
Very common: ≥1/10	Pain at injection site, fatigue	General disorders and administration site conditions
	Headache	Nervous system disorders
	Myalgia	Musculoskeletal and connective tissue disorders

Common: ≥1/100 to <1/10	Malaise, chills,	General disorders and administration site conditions
	Arthralgia	Musculoskeletal and connective tissue disorders

OVERDOSE

Overdose is considered highly unlikely due to the presentation of **Pertagen®** in monodose pre-filled syringe.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties

Pharmaco-therapeutic group: Bacterial vaccines, ATC code: J07AJ02

Immunogenicity of **Pertagen®** was evaluated in 150 adolescents aged 12 – 27 years old and compared with a licensed Tdap vaccine to show non-inferiority (Committee for Medicinal Products for Human Use (CHMP) (2005) Guideline on the choice of the non-inferiority margin: EMEA/CPMP/EWP/2158/99).

At 28 days after vaccination, ELISA anti-PT and anti-FHA antibody titers and seroconversion rates were statistically significant higher in subjects vaccinated with Pertagen® than in subjects vaccinated with the licensed Tdap vaccine. Non-inferiority of **Pertagen®** was met. In addition, superiority of ELISA anti-PT and anti-FHA seroconversion rates and GMTs was demonstrated according to EMEA guidelines (Committee for Proprietary Medicinal Products (CPMP) (2000) Points to consider on switching between superiority and non-inferiority: CPMP/EWP/482/99).

Non-inferiority test for seroconversion rates of anti-PT and anti-FHA antibody titers as assessed by ELISA in Pertagen® *vs* a licensed Tdap vaccine in 12 – 17 years old adolescents

Seroconversion rates [a]	**Pertagen® (N=148)**	**Licensed Tdap (N=149)**	**Difference [b]**
	n (%)	n (%)	% (95% CI)
PT	142 (95.95)	82 (55.03)	40.91 (32.32 – 49.51)
FHA	138 (93.24)	81 (54.36)	38.88 (29.92 – 47.84)

a: Seroconversion defined as ≥ 4 fold increase at 28 days after vaccination as compared to baseline titers

b: Based on non-inferiority test with different margin of 10%

Non-inferiority test for anti-PT and anti-FHA GMTs as assessed by ELISA in Pertagen® *vs* a licensed Tdap vaccine in 12 – 17 years old adolescents

Geometric Mean	Pertagen®	Licensed Tdap	GMT Ratio [b] (95% CI)
	GMT [a] (IU/mL) (95% CI)	GMT [a] (IU/mL) (95% CI)	
PT	527.51 (435.57 – 638.87)	48.09 (36.99 – 62.50)	10.97 (8.39 – ∞)
FHA	836.13 (725.13 – 964.12)	178.19 (148.94 – 213.19)	4.69 (3.88 – ∞)

a: Geometric Mean Change from baseline at Day 28 after vaccination
b: Based on non-inferiority test with GMT Ratio > 0.67

Protective efficacy of pertussis

No established correlates of protection to pertussis antigens are currently available. Although efficacy or effectiveness data of **Pertagen®** are not available for adolescents and adults including pregnant women, non-inferiority of the immune response of **Pertagen®** was demonstrated as per WHO recommendations (TRS 979, 2013) in adolescents in a comparative randomized controlled trial with a licensed Tdap vaccine evaluated in effectiveness study. The antibody titers to pertussis antigens, PT and FHA, after vaccination with **Pertagen®** were statistically higher than those observed after immunization with the Tdap comparator vaccine. In addition, 1 month after booster vaccination, the neutralizing antibodies against PT antigen were also significantly higher with **Pertagen®** than with the Tdap comparator vaccine.

Pharmacokinetic properties

Evaluation of pharmacokinetic properties is not required for vaccines.

Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies of safety and toxicity.

STORAGE CONDITIONS

Pertagen® should be stored at 2°C to 8°C. Do not freeze. Discard if vaccine has been frozen. Store in the original package in order to protect from light.
Keep out of the sight and reach of children.

SHELF-LIFE

3 years.

EXPIRY DATE

The expiry date of **Pertagen®** is indicated on the label and packaging.

PRESENTATION

Single-dose (0.5 mL) pre-filled syringe which is made of a type I glass, conforming to European Pharmacopoeia requirements. The container closure system of **Pertagen®** is free of latex.

BioNet

Manufactured by BioNet-Asia Co., Ltd., Hi-Tech Industrial Estate, 81 Moo 1, Bang Pa-In, Ayutthaya 13160, Thailand

Marketing Authorization Number: SIN16283P

Date of Revision of Package Insert: 23 July 2021