BOOSTRIX

Version GDSv11-IPIv12

BOOSTRIX

Diphtheria, tetanus and pertussis vaccine (acellular component) (adsorbed, reduced antigenic content)

Suspension for injection

Qualitative and Quantitative Composition

1 serving (0.5 ml) contains:

Diphtheria toxoid[1]	not less than 2 international units (IU) (2.5 Lf)
TETANIC TOXOID[1]	not less than 20 international units (IU) (5 Lf)
Bordetella pertussis antigens	
Pertussis toxoid[1]	8 micrograms
Filamentous hemagglutinin[1]	8 micrograms
Pertactin[1]	2.5 micrograms
[1] adsorbed in aluminum hydroxide, hydrated (Al(OH)3), 0.3 milligrams Al^{3+} aluminum phosphate ($AlPO_4$), 0.2 milligrams Al^{3+}	

BOOSTRIX is a cloudy white suspension. When stored, a white deposit and a transparent supernatant may form. This is a normal result.

Clinical Information

Directions

BOOSTRIX is indicated for booster vaccination against diphtheria, tetanus and pertussis in individuals four years of age and older (see *Dosage*).

BOOSTRIX is also indicated for passive protection against pertussis in early childhood after maternal immunisation during pregnancy (see DOSAGE, PREGNANCY AND PHARMACODYNAMICS).

The use of ***BOOSTRIX*** should comply with official recommendations.

Dosage and Administration

Dosage

A single 0.5 ml dose of the vaccine is recommended.

BOOSTRIX can be administered according to usual local medical practice for booster vaccination with reduced content diphtheria-tetanus combination vaccine, when a pertussis booster dose is required.

BOOSTRIX may be administered to adolescents and adults whose vaccination status is unknown or who have incomplete vaccination against diphtheria, tetanus and pertussis, as part of an immunization series against diphtheria, tetanus and pertussis (see section *Pharmacodynamics*). Based on adult data, two additional doses of diphtheria and tetanus vaccine are recommended one and six months after the first dose to maximize the diphtheria-tetanus vaccine response.

Repeat vaccination against diphtheria, tetanus and pertussis should be carried out at intervals according to official recommendations (usually 10 years).

BOOSTRIX can be administered to pregnant women during the second or third trimester according to official recommendations (see Indications, Pregnancy and Pharmacodynamics).

BOOSTRIX can also be used in the management of wounds with potential tetanus infection in people who have previously received a primary vaccination series with tetanus toxoid vaccine. Tetanus immunoglobulin should be administered concomitantly in accordance with official recommendations.

Method of Administration

BOOSTRIX is for deep intramuscular injection, preferably in the deltoid region (see also section *Warnings and precautions*).

Contraindications

BOOSTRIX must not be administered to subjects with hypersensitivity to any of the components of the vaccine (see *QUALITATIVE AND QUANTITATIVE COMPOSITION AND List of excipients*) or to subjects who have shown signs of hypersensitivity after prior administration of diphtheria, tetanus or pertussis vaccines.

BOOSTRIX is contraindicated if the subject has suffered from an encephalopathy of unknown etiology during the seven days following a previous vaccination with pertussis vaccines. In these circumstances, pertussis vaccination should be discontinued and the vaccination course with diphtheria and tetanus vaccines should be continued.

BOOSTRIX should not be administered to subjects who have had transient thrombocytopenia or neurological complications following a previous immunisation against diphtheria and/or tetanus (for information on seizures or hypotonic-hyporeactive episodes, see *WARNINGS AND PRECAUTIONS*).

Warnings and Precautions

As with other vaccines, administration of ***BOOSTRIX*** should be postponed in subjects suffering from severe acute febrile illness. However, the presence of a mild infection is not a contraindication to the vaccine.

Before vaccination, medical history (especially regarding previous vaccination and the possible occurrence of undesirable reactions) should be reviewed and a clinical examination performed.

If any of the following events occurred in temporal relation to the administration of the vaccine containing the pertussis component, subsequent administration of doses of pertussis vaccines should be carefully considered:

- temperature 40.0 °C within 48 hours after vaccination, not due to another identifiable cause;≥
- Collapse or shock-like state (hypotonic-hyporeactive episode) within 48 hours;
- persistent, inconsolable crying lasting 3 hours within 48 hours of vaccination;≥
- seizures, whether or not accompanied by fever, within 3 days of vaccination.

In children with progressive neurological problems, including infantile spasms, uncontrolled epilepsy or progressive encephalopathy, it is preferable to delay immunization against pertussis (acellular or whole cell pertussis) until the underlying disease has been corrected or stabilized. However, the decision to administer pertussis vaccine should be made on a case-by-case basis after carefully determining the risks and benefits.

As with all injectable vaccines, appropriate medical treatment and supervision should be available at all times in the event of a rare anaphylactic reaction following administration of the vaccine.

BOOSTRIX should be administered with caution in people with thrombocytopenia or bleeding disorders, as bleeding may occur after intramuscular administration in these patients. If according to official recommendations, it may be necessary to administer the vaccine subcutaneously to these individuals. With both routes of administration,firm pressure should be applied to the injection site (without rubbing) for at least two minutes.

A history or family history of seizures and a family history of adverse reactions following DTP vaccination are not contraindications.

Human immunodeficiency virus (HIV) infection is not considered a contraindication to vaccination against diphtheria, tetanus and pertussis. The expected immune response may not be obtained after vaccination of immunosuppressed patients.

Extremely rarely, cases of collapse or shock-like state (hypotonic-hyporeactive episode) and seizures have been reported within 2 to 3 days of vaccination with DTaP vaccines and DTaP combination vaccines.

***Under* no circumstances should BOOSTRIX be administered intravascularly.**

Syncope (fainting) may occur after, or even before, any vaccination as a psychogenic response to needle injection. It is important that proper procedures are available to prevent fainting injuries.

As with any vaccine, a protective immune response may not be achieved in all vaccinated subjects.

Interactions

Concomitant use with other inactivated vaccines and immunoglobulin is unlikely to interfere with immune responses.

When deemed necessary, ***BOOSTRIX*** may be administered simultaneously with other vaccines or immunoglobulins.

If ***BOOSTRIX*** is given at the same time as another vaccine or immunoglobulin injection, the products should always be given in different locations.

As with other vaccines, patients being treated with immunosuppression therapy or immunodeficiency may not have an adequate response. In these patients, when a tetanus vaccine is needed for a wound with a possibility of tetanus infection, a tetanus-only vaccine should be used.

Pregnancy and Lactation

Fertility

No data are available on humans. Animal studies do not indicate direct or indirect harmful effects related to female fertility.

Pregnancy

Boostrix can be used during the second or third trimester of pregnancy according to official recommendations.

For data regarding the prevention of pertussis disease in infants born to women vaccinated during pregnancy, see *the section Pharmacodynamics.*

Safety data resulting from a randomized, controlled clinical trial (341 pregnancy outcomes) and a prospective observational study (793 pregnancy outcomes) in which Boostrix was administered to pregnant women during the third trimester have not demonstrated any vaccine-related adverse reactions to pregnancy or fetus/newborn health.

Safety data resulting from prospective clinical studies on the use of Boostrix or Boostrix Polio during the first and second trimesters of pregnancy are not available.

Postmarketing surveillance data in which pregnant women were exposed to Boostrix or Boostrix Polio (dTpa-IPV vaccine) in the second or third trimester demonstrated no vaccine-related adverse effects on pregnancy or fetus/newborn health.

As with other inactivated vaccines, vaccination with Boostrix is not expected to affect the fetus in any trimester of pregnancy.

Animal studies do not indicate direct or indirect harmful effects related to pregnancy, embryonic/foetal development, parturition or postnatal development.

Nursing

The safety of ***BOOSTRIX*** when administered to lactating women has not been evaluated.

It is unknown whether ***BOOSTRIX*** is excreted in human human breast milk.

BOOSTRIX should be used during breastfeeding only when the potential benefits outweigh the potential risks.

Effects on the Ability to Drive and Use Machines

The vaccine is unlikely to have an effect on the ability to drive and use machines.

Adverse Reactions

Clinical Trial Data

The safety profile presented below is based on data from clinical trials in which ***BOOSTRIX*** was administered to 839 children (4 to 9 years of age) and 1931 adults, adolescents and children (over 10 years of age).

Reported adverse reactions are indicated according to the following frequency:

Very common1/10 ≥
Common1/100 and <1/10 ≥
Uncommon1/1000 and <1/100 ≥
Rare1/10000 and <1/1000 ≥
Very rare<1/10000

Children 4 to 9 years old

Infections and Infestations

Uncommon upper respiratory tract infection

Metabolic and Nutrition Disorders

Frequentsanorexia

Psychiatric Disorders

Very commonirritability

Nervous System Disorders

Very commondrowsiness
Commonheadache
Uncommonimpaired attention

Eye Disorders

Uncommonconjunctivitis

Gastrointestinal Disorders

Commondiarrhoea, vomiting, gastrointestinal disturbances

Skin and Subcutaneous Tissue Disorders

Uncommonrashrash

General Disorders and Conditions at the Site of Administration

Very commoninjection site reactions (including pain, redness, and swelling), fatigue
Commonfever ≥ 37.5 °C (including fever > 39 °C)
Uncommonother injection site reactions (such as induration), pain

Adults, Teens and Children 10 Years of Age and Older

Infections and Infestations

Uncommon: upper respiratory tract infection, pharyngitis

Blood and Lymphatic System Disorders

Uncommonlymphadenopathy

Nervous System Disorders

Very commonheadache
Frequent dizziness
Uncommonsyncope

Respiratory, Thoracic and Mediastinal Disorders

Uncommon

Gastrointestinal Disorders

Commonnausea, gastrointestinal disorders
Uncommondiarrhea, vomiting

Skin and Subcutaneous Tissue Disorders

Uncommonhyperhidrosis, pruritus, rash

Musculoskeletal and Connective Tissue Disorders

Uncommonarthralgia, myalgia, joint stiffness, musculoskeletal stiffness

General Disorders and Conditions at the Site of Administration

Very commoninjection site reactions (including pain, redness, and swelling), fatigue, malaise
Commonfever ≥ 37.5 °C, injection site reactions (such as injection site mass and sterile injection site abscess)
Uncommonfever > 39°C, influenza-like illness, pain

Reactogenicity After Repeated Dosing of *BOOSTRIX*

Data obtained from 146 subjects suggest that with repeated vaccination according to a schedule of 0, 1, 6 months in adults (> 40 years of age) a small increase in local reactogenicity (pain, redness, inflammation) occurs.

Subjects with complete primary vaccination of 4 doses of DTPw followed by one dose of BOOSTRIX at approximately 10 years of age showed increased local reactogenicity after an additional dose of ***BOOSTRIX*** administered 10 years later.

Post-Marketing Data

Blood and Lymphatic System Disorders

Rare angioedema

Immune System Disorders

Very rareallergic reactions, including anaphylactic and anaphylactoid reactions

Nervous System Disorders

Rare seizures (with or without fever)

Skin and Subcutaneous Tissue Disorders

Rarasurticaria

General Disorders and Conditions at the Site of Administration

Raregeneralized inflammation in the limb where the vaccine was given, asthenia

Overdose

Cases of overdose have been reported during post-marketing surveillance. Adverse events following overdose, when reported, were similar to those reported following normal administration of the vaccine.

Pharmacological properties

Pharmacodynamics

Pharmaco-therapeutic group: combined bacterial vaccines, ATC code J07AJ52

Immune response

Approximately one month after booster vaccination with ***BOOSTRIX***:

- The rate of seropositivity/seroprotection against the different components of the vaccine was at least 99% in children 4 to 9 years of age.
- The rate of seropositivity/seroprotection against the different components of the vaccine was at least 97% in adults and adolescents from 10 years of age.

The results of comparative studies with commercial dT vaccines indicate that the degree and duration of protection are not different from those obtained with these vaccines.

Protective Efficacy Against Whooping Cough

There is currently no defined protective correlate for whooping cough; however, the protective efficacy of GlaxoSmithKline Biologicals (Infanrix) DTaP against WHO-defined typical pertussis (21 days of paroxysmal cough with laboratory confirmation) was demonstrated in the following studies of three primary doses:≥

- A prospective blinded study of household contacts conducted in Germany (3, 4, 5 month schedule). Data collected from secondary contacts in households where there was an index case with typical pertussis indicate that the protective efficacy of the vaccine was 88.7%. Protection against mild laboratory-confirmed illness, defined as 14 or more days of cough of any type, was 73%, and 67% when defined as 7 or more days of cough of any type.
- An efficacy study subsidized by the NIH (National Institute of Health) conducted in Italy (2, 4, 6 month schedule). The efficacy of the vaccine was found to be 84%. When the definition of pertussis was expanded to include milder clinical cases with respect to the type and duration of cough, the efficacy of Infanrix was calculated.
- It was 71% versus >7 days of any cough and 73% versus >14 days of any cough.

Vaccinees given ***BOOSTRIX*** had pertussis antibody titers higher than those in the household contact study in Germany, where protective efficacy was 88.7%.

Passive protection against pertussis in infants (less than 3 months of age) born to mothers vaccinated during pregnancy

A randomized, crossover, placebo-controlled study demonstrated higher concentrations of pertussis antibodies during delivery in the umbilical cord blood of infants born to mothers vaccinated with Boostrix (N = 291) versus placebo (N = 292) during the third trimester of pregnancy. Concentrations of antibodies against pertussis antigens PT, FHA, and PRN were respectively 9, 16, and 21 times higher in the umbilical cord blood of infants bornto vaccinated mothers than control infants. These antibody titers could provide passive protection against pertussis, as evidenced by observational effectiveness studies.

Immunogenicity in infants and young children born to mothers vaccinated during pregnancy

In follow-up trials of more than 500 infants and toddlers born to vaccinated mothers, clinical data showed no clinically relevant interference between maternal vaccination with Boostrix and the infant's or toddler's response to diphtheria, tetanus, hepatitis B, inactivated polio virus, *Haemophilus influenzae* Type B or pneumococcal antigens. Although lower concentrations of antibodies against some pertussis antigens were observed after primary and booster vaccination, 92.1-98.1% of individuals born to vaccinated mothers showed a booster response against all pertussis antigens. whooping cough. Current epidemiological data on pertussis do not suggest any clinical relevance of this immune interference.

Effectiveness in protecting against pertussis disease in infants born to women vaccinated during pregnancy

The effectiveness of the BOOSTRIX or ***BOOSTRIX*** Polio vaccine (EV) was evaluated in three observational studies, in the United Kingdom, Spain and Australia. The vaccine was used during the third trimester of pregnancy to protect infants younger than 3 months of age against pertussis disease as part of a maternal vaccination program.

Details of each study's design and results are given in the table below.

EV against pertussis disease for infants less than 3 months of age born to mothers vaccinated during the third trimester of pregnancy with BOOSTRIX/*BOOSTRIX* Polio

Place of study	Vaccine	Study design	Vaccine effectiveness
United Kingdom	***BOOSTRIX*** Polio	Retrospective, detection method	88% (95% CI: 79, 93)
Spain	***BOOSTRIX***	Prospective, cases and matched controls	90.9% (95% CI: 56.6, 98.1)
Australia	***BOOSTRIX***	Prospective, cases and matched controls	69% (95% CI: 13, 89)
CI: confidence interval			

If maternal vaccination occurs within two weeks before delivery, the effectiveness of the vaccine in the infant may be lower than the numbers in the table.

Persistence of the Immune Response

Five to six years after vaccination with ***BOOSTRIX***, at least 94% of children 4 years of age and older were seroprotected or seropositive against all components of the vaccine, except for the toxoid component of pertussis (52% of subjects were seropositive against pertussis toxoid).

Ten years after vaccination with ***BOOSTRIX***, at least 86% of adults were seroprotected or seropositive against all components of the vaccine.

In adolescents, the percentage of subjects who were seroprotected or seropositive was at least 82% against all components of the vaccine, except for the pertussis toxoid component (61% of subjects were seropositive against pertussis toxoid).

Immune Response After Repeated Dosing of *BOOSTRIX*

The immunogenicity of ***BOOSTRIX***, administered 10 years after a previous booster dose with a reduced antigen-containing diphtheria(s), tetanus, and anti-pertussis vaccine(s), has been evaluated. One month after vaccination, > 99% of subjects were seroprotected against diphtheria and tetanus and seropositive against pertussis.

Immune Response in Subjects with No Prior Vaccination History or Unknown Vaccination History

In adolescents 11 to 18 years of age, with no prior pertussis vaccination and no diphtheria/tetanus vaccination in the previous 5 years, one dose of ***BOOSTRIX*** induced an immune response to pertussis and all subjects were protected against tetanus and diphtheria.

In subjects 40 years of age who had not received any diphtheria or tetanus vaccine in the past 20 years (including those who had never been vaccinated before or whose vaccination history was unknown), one dose of ≥***BOOSTRIX*** induced in most cases an immune response to pertussis and protected against tetanus and diphtheria.

Preclinical Safety Data

Toxicology and/or Pharmacology in Animals

Preclinical data show no special risks to humans based on conventional safety and toxicity studies.

Pharmaceutical Characteristics

List of Excipients

Sodium chloride, water for injection.

As residues of the manufacturing process are present the following substances: formaldehyde, polysorbate 80, glycine.

Expiration Period

The expiration date of the vaccine is indicated on the label and packaging.

Special Storage Precautions

Store in a refrigerator (2C – 8C). °°**Do not freeze.** If it has been frozen, it should be discarded.

Protect from light.

The storage conditions are detailed on the packaging.

Nature and Content of the Container

BOOSTRIX is supplied as a cloudy white suspension in a single-dose glass ampoule or prefilled syringe.

The ampoules and prefilled syringes are made of type I neutral glass, which meets the requirements of the European Pharmacopoeia.

Not all presentations exist in all countries.

Incompatibilities

Boostrix must not be mixed with other vaccines in the same syringe.

Instructions for Use/Handling

Prior to administration, the vaccine should be shaken well to obtain a cloudy and homogeneous white suspension and visually inspected for any foreign particulate matter and physical variation. If any of these things are observed, the vaccine should not be administered.

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

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