# Boostrix Polio

## 1. NAME OF THE MEDICINAL PRODUCT

Boostrix Polio

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 dose (0.5 ml) contains:

| | |
|---|---|
| Diphtheria toxoid[1] | not less than 2 International Units (IU) (2.5 Lf) |
| Tetanus toxoid[1] | not less than 20 International Units (IU) (5 Lf) |
| *Bordetella pertussis* antigens | |
| Pertussis toxoid[1] | 8 micrograms |
| Filamentous Haemagglutinin[1] | 8 micrograms |
| Pertactin[1] | 2.5 micrograms |
| Inactivated poliovirus | |
| type 1 (Mahoney strain)[2] | 40 D-antigen unit |
| type 2 (MEF-1 strain)[2] | 8 D-antigen unit |
| type 3 (Saukett strain)[2] | 32 D-antigen unit |

| | |
|---|---|
| [1]adsorbed on aluminium hydroxide, hydrated ($Al(OH)_3$) | 0.3 milligrams $Al^{3+}$ |
| and aluminium phosphate ($AlPO_4$) | 0.2 milligrams $Al^{3+}$ |

[2] propagated in VERO cells

The vaccine may contain traces of formaldehyde, neomycin and polymyxin which are used during the manufacturing process (see section 4.3).

Excipients with known effect
The vaccine contains para-aminobenzoic acid < 0.07 nanograms per dose and phenylalanine 0.0298 micrograms per dose (see section 4.4).

For the full list of excipients, see section 6.1

## 3. PHARMACEUTICAL FORM

Suspension for injection in pre-filled syringe.

Boostrix Polio is a turbid white suspension.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Boostrix Polio is indicated for booster vaccination against diphtheria, tetanus, pertussis and poliomyelitis of individuals from the age of three years onwards (see section 4.2).

The administration of Boostrix Polio should be based on official recommendations.

## 4.2 Posology and method of administration

Posology

A single 0.5 ml dose of the vaccine is recommended.

Boostrix Polio may be administered from the age of three years onwards.

The use of Boostrix-IPV may be considered during the third trimester of pregnancy. For the use of the vaccine before the third trimester of pregnancy, see section 4.6.

Boostrix Polio contains reduced content of diphtheria, tetanus and pertussis antigens in combination with poliomyelitis antigens. Therefore, Boostrix Polio should be administered in accordance with official recommendations and/or local practice.

Boostrix Polio may also be administered to adolescents and adults with unknown vaccination status or incomplete vaccination against diphtheria, tetanus and pertussis as part of an immunisation series against diphtheria, tetanus, pertussis and poliomyelitis. Based on data in adults, two additional doses of a diphtheria and tetanus containing vaccine are recommended one and six months after the first dose to maximize the vaccine response against diphtheria and tetanus (see section 5.1).

Boostrix Polio can be used in the management of tetanus prone injuries in persons who have previously received a primary vaccination series of tetanus toxoid vaccine and for whom a booster against diphtheria, pertussis and poliomyelitis is indicated. Tetanus immunoglobulin should be administered concomitantly in accordance with official recommendations.

Repeat vaccination against diphtheria, tetanus, pertussis and poliomyelitis should be performed at intervals as per official recommendations.

*Paediatric population*

The safety and efficacy of Boostrix Polio in children below 3 years of age have not been established.

Method of administration

Boostrix Polio is for deep intramuscular injection preferably in the deltoid region (see section 4.4).

## 4.3 Contraindications

Hypersensitivity to the active substances or to any of the excipients listed in section 6.1 or to neomycin, polymyxin or formaldehyde.

Hypersensitivity after previous administration of diphtheria, tetanus, pertussis or poliomyelitis vaccines.

Boostrix Polio is contraindicated if the subject has experienced an encephalopathy of unknown aetiology, occurring within 7 days following previous vaccination with pertussis-containing vaccine. In these circumstances, pertussis vaccination should be discontinued and the vaccination course should be continued with diphtheria, tetanus and poliomyelitis vaccines.

Boostrix Polio should not be administered to subjects who have experienced transient thrombocytopenia or neurological complications (for convulsions or hypotonic-hyporesponsive episodes, see section 4.4) following an earlier immunisation against diphtheria and/or tetanus.

As with other vaccines, administration of Boostrix Polio should be postponed in subjects suffering

from acute severe febrile illness. The presence of a minor infection is not a contraindication.

## 4.4 Special warnings and precautions for use

Vaccination should be preceded by a review of the medical history (especially with regard to previous vaccination and possible occurrence of undesirable events).

If any of the following events are known to have occurred in temporal relation to receipt of pertussis-containing vaccine, the decision to give doses of pertussis-containing vaccines should be carefully considered:

- Temperature of ≥ 40.0°C within 48 hours of vaccination, not due to another identifiable cause.
- Collapse or shock-like state (hypotonic-hyporesponsiveness episode) within 48 hours of vaccination.
- Persistent, inconsolable crying lasting ≥ 3 hours, occurring within 48 hours of vaccination.
- Convulsions with or without fever, occurring within 3 days of vaccination.

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

As for any vaccination, the risk-benefit of immunising with Boostrix Polio or deferring this vaccination should be weighed carefully in a child suffering from a new onset or progression of a severe neurological disorder.

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

Boostrix Polio should be administered with caution to subjects with thrombocytopenia (see section 4.3) or a bleeding disorder since bleeding may occur following an intramuscular administration to these subjects. Firm pressure should be applied to the injection site (without rubbing) for at least two minutes.

Boostrix Polio should in no circumstances be administered intravascularly.

A history of febrile convulsions, a family history of convulsions and a family history of an adverse event following DTP vaccination do not constitute contraindications.

Human Immunodeficiency Virus (HIV) infection is not considered as a contraindication. The expected immunological response may not be obtained after vaccination of immunosuppressed patients.

Syncope (fainting) can occur following, or even before, any vaccination especially in adolescents as a psychogenic response to the needle injection. This can be accompanied by several neurological signs such as transient visual disturbance, paraesthesia and tonic-clonic limb movements during recovery. It is important that procedures are in place to avoid injury from faints.

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

Excipients with known effect
Boostrix Polio contains para-aminobenzoic acid. It may cause allergic reactions (possibly delayed), and exceptionally, bronchospasm.

This medicine contains 0.0298 micrograms phenylalanine in each dose. Phenylalanine may be harmful if you have phenylketonuria (PKU), a rare genetic disorder in which phenylalanine builds up because the body cannot remove it properly.

This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.
This medicine contains potassium, less than 1 mmol (39 mg) per dose, i.e. essentially 'potassium-

free'.

Traceability

In order to improve the traceability of biological medicinal products, the name of the administered product should be clearly recorded. It is recommended to record the batch number as well.

## 4.5 Interaction with other medicinal products and other forms of interaction

**Use with other vaccines or immunoglobulins**

Boostrix-Polio may be administered concomitantly with any of the following monovalent or combination vaccines: measles, mumps, rubella, varicella (MMR/V) and human papilloma virus (HPV) vaccine with no clinically relevant interference with antibody response to any of the components of either vaccine (see section 4.8).

Concomitant administration of Boostrix Polio with other vaccines or with immunoglobulins has not been studied.
It is unlikely that co-administration will result in interference with the immune responses.

According to generally accepted vaccine practices and recommendations, if concomitant administration of Boostrix Polio with other vaccines or immunoglobulins is considered necessary, the products should be given at separate sites.

**Use with immunosuppressive treatment**

As with other vaccines, patients receiving immunosuppressive therapy may not achieve an adequate response.

## 4.6 Fertility, pregnancy and lactation

**Pregnancy**

The use of Boostrix-Polio may be considered during the third trimester of pregnancy.

For data relating to the prevention of pertussis disease in infants born to women vaccinated during pregnancy, see section 5.1.

Safety data from a prospective observational study where Boostrix (dTpa component of Boostrix-Polio) was administered to pregnant women during the third trimester (793 pregnancy outcomes) as well as data from passive surveillance where pregnant women were exposed to Boostrix-Polio or to Boostrix in the 3$^{rd}$ and 2$^{nd}$ trimester have shown no vaccine related adverse effect on pregnancy or on the health of the foetus/newborn child.

Human data from prospective clinical studies on the use of Boostrix-Polio during the first and second trimester of pregnancy are not available. However, as with other inactivated vaccines, it is not expected that vaccination with Boostrix-Polio harms the foetus at any trimester of pregnancy. The benefits versus the risks of administering Boostrix-IPV during pregnancy should be carefully evaluated.

Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or post-natal development (see section 5.3).

Limited data indicate that maternal antibodies may reduce the magnitude of the immune response to some vaccines in infants born from mothers vaccinated with Boostrix-IPV during pregnancy. The clinical relevance of this observation is unknown.

**Breastfeeding**

The effect of administration of Boostrix Polio during lactation has not been assessed. Nevertheless, as Boostrix Polio contains toxoids or inactivated antigens, no risk to the breastfed infant should be expected. The benefits versus the risk of administering Boostrix Polio to breastfeeding women should carefully be evaluated by the healthcare providers.

**Fertility**

No human data from prospective clinical studies are available. Animal studies do not indicate direct or indirect harmful effects with respect to female fertility (see section 5.3).

## 4.7 Effects on ability to drive and use machines

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

## 4.8 Undesirable effects

***Summary of the safety profile***

The safety profile presented in Table 1 is based on data from clinical trials where Boostrix Polio was administered to 908 children (from 4 to 8 years of age) and 955 adults, adolescents and children (from 10 to 93 years of age).

The most common events occurring after Boostrix Polio administration in both groups were local injection site reactions (pain, redness and swelling) reported by 31.3 – 82.3% of subjects overall. These usually had their onset within the first 48 hours after vaccination. All resolved without sequelae.

***Tabulated list of adverse reactions***
Adverse reactions reported 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)
Very rare: (< 1/10,000)

- **Clinical trials**

**Table 1:** Adverse reactions reported in clinical trials with Boostrix-Polio

| ***System Organ Class*** | ***Frequency*** | ***Adverse reactions*** | |
|---|---|---|---|
| | | ***Subjects aged 4 - 8 years (N=908)*** | ***Subjects aged 10 - 93 years (N = 955)*** |
| ***Infections and infestations*** | Uncommon | | oral herpes |
| ***Blood and lymphatic system disorders*** | Uncommon | lymphadenopathy | lymphadenopathy |
| ***Metabolism and nutrition disorders*** | Common | anorexia | |

| | | | |
|---|---|---|---|
| | Uncommon | | decreased appetite |
| ***Psychiatric disorders*** | Common | irritability | |
| | Uncommon | sleep disorder, apathy | |
| ***Nervous system disorders*** | Very common | somnolence | headache |
| | Common | headache | |
| | Uncommon | | paraesthesia, somnolence, dizziness |
| ***Respiratory, thoracic and mediastinal disorders*** | Uncommon | dry throat | asthma |
| ***Gastrointestinal disorders*** | Common | | gastrointestinal disorders (such as vomiting, abdominal pain, nausea) |
| | Uncommon | diarrhoea, vomiting, abdominal pain, nausea | |
| ***Skin and subcutaneous tissue disorders*** | Uncommon | | pruritus |
| ***Musculoskeletal and connective tissue disorders*** | Uncommon | | arthralgia, myalgia |
| ***General disorders and administration site conditions*** | Very common | injection site reactions (such as redness and/or swelling), injection site pain | injection site reactions (such as redness and/or swelling), fatigue, injection site pain |
| | Common | pyrexia (fever ≥ 37.5°C, including fever > 39°C), extensive swelling of vaccinated limb (sometimes involving the adjacent joint), injection site reactions (such as haemorrhage, pruritus and induration) | pyrexia (fever ≥ 37.5°C), injection site reactions (such as haematoma, pruritus, induration and warmth numbness) |
| | Uncommon | fatigue | extensive swelling of vaccinated limb (sometimes involving the adjacent joint), pyrexia (fever > 39.0°C), chills, pain |

*Coadministration with MMR/V vaccines in children aged 3-6 years*

Boostrix-Polio was coadministered with MMR/V vaccines in 2 clinical studies with 406 children aged 3-6 years. In these studies, upper respiratory tract infection and rash were commonly reported. Fever, irritability, fatigue, loss of appetite and gastrointestinal disorders (including diarrhoea and vomiting) were reported with a higher frequency (very common) when compared to Table 1 while all other adverse reactions occurred at the same or lower frequency.

Adverse reactions additionally reported during clinical studies with Boostrix (dTpa component of

Boostrix-Polio), administered to 839 children (from 4 to 8 years of age) and 1931 adults, adolescents and children (from 10 to 76 years of age), are listed in Table 2.

**Table 2**: Adverse reactions reported in clinical trials with Boostrix

| ***System Organ Class*** | ***Frequency*** | ***Adverse reactions*** | |
|---|---|---|---|
| | | ***Subjects aged 4 - 8 years (N=839)*** | ***Subjects aged 10 - 76 years (N = 1931)*** |
| ***Infections and infestations*** | Uncommon | | upper respiratory tract infection, pharyngitis |
| ***Nervous system disorders*** | Uncommon | disturbances in attention | syncope |
| ***Eye disorders*** | Uncommon | conjunctivitis | |
| ***Respiratory, thoracic and mediastinal disorders*** | Uncommon | | cough |
| ***Gastrointestinal disorders*** | Uncommon | | diarrhoea |
| ***Skin and subcutaneous tissue disorders*** | Uncommon | | hyperhidrosis, rash |
| ***Musculoskeletal and connective tissue disorders*** | Uncommon | | joint stiffness, musculoskeletal stiffness |
| ***General disorders and administration site conditions*** | Very common | | malaise |
| | Common | | injection site reactions (such as injection site mass and injection site abscess sterile) |
| | Uncommon | pain | influenza like illness |

*Reactogenicity after repeat dose*

Data suggest that in subjects primed with DTP in childhood a second booster dose might give an increase of local reactogenicity.

Subjects aged 15 years onwards without recent vaccination for diphtheria, tetanus, pertussis and poliomyelitis, who received a dose of Boostrix-Polio or another reduced-antigen content vaccine, followed by an additional dose of Boostrix-Polio 10 years after, showed no increased reactogenicity after this second dose compared to the first one.

- **Post-marketing surveillance**

Because these events were reported spontaneously, it is not possible to reliably estimate their frequency.

**Table 3:** Adverse reactions reported with Boostrix-Polio during post-marketing surveillance

| ***System Organ Class*** | ***Frequency*** | ***Adverse reactions*** |
|---|---|---|
| ***Immune system disorders*** | unknown | allergic reactions, including anaphylactic and anaphylactoid reactions |

| | | |
|---|---|---|
| ***Nervous system disorders*** | unknown | hypotonic-hyporesponsiveness episodes, convulsions (with or without fever) |
| ***Skin and subcutaneous tissue disorders*** | unknown | urticaria, angioedema |
| ***General disorders and administration site conditions*** | unknown | asthenia |

Following administration of tetanus toxoid containing vaccines, there have been very rare reports of adverse reactions on the central or peripheral nervous systems, including ascending paralysis or even respiratory paralysis (e.g. Guillain-Barré syndrome).

**Reporting of suspected adverse reactions**
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il/
Additionally, you should also report to GSK Israel, (il.safety@gsk.com).

### 4.9 Overdose

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

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Bacterial and viral vaccines combined, ATC code: J07CA02

*Immune response*

The immune responses to Boostrix Polio were evaluated in clinical trials carried out in subjects of different ages having different vaccination histories (see section 4.8).

The following immune responses were observed across studies one month post vaccination with Boostrix-Polio in children, adolescents and adults (Table 4).

**Table 4**: Immune response in children, adolescents and adults

| **Antigen** | Response | **Children aged 3 to 8 years**<br>**N=1195**<br>(% vaccinees) | **Adults, adolescents and children aged from 10 years onwards**<br>**N=923**<br>(% vaccinees) |
|---|---|---|---|
| **Diphtheria** | ≥ 0.1 IU/ml | 100% | 82.2 – 100% |
| | ≥ 0.016 IU/ml [(1)] | NA | 87.7 – 100% [(2)] |
| **Tetanus** | ≥ 0.1 IU/ml | 99.9 – 100% | 99.6 – 100% |
| **Pertussis** | Booster response [(3)] | | |
| Pertussis toxoid | | 84.6 – 90.6% | 79.8 – 94.0% |
| Filamentous haemagglutinin | | 90.1 – 98.8% | 90.7 – 97.2% |
| Pertactin | | 94.2 – 96.6% | 90.0 – 96.7% |
| **Inactivated poliovirus** | ≥8 ED50 | | |
| type 1 | | 98.8 – 100% | 99.6 – 100% |
| type 2 | | 99.2 – 100% | 99.6 – 100% |
| type 3 | | 99.4 – 100% | 99.1 – 100% |

N=number of subjects

(1) Percentage of subjects with antibody concentrations associated with protection against disease (≥ 0.1 IU/ml by ELISA assay or ≥ 0.016 IU/ml by an in-vitro Vero-cell neutralisation assay).

(2) This assay was not performed in study HPV-042.

(3) Booster response defined as:

- for initially seronegative subjects, antibody concentrations at least four times the cut-off (post-vaccination concentration ≥ 20 El.U/ml);
- for initially seropositive subjects with Pre booster vaccination concentration ≥ 5 El.U/ml and < 20 El.U/ml: an increase in antibody concentrations of at least four times the Pre booster vaccination concentration.
- for initially seropositive subjects with Pre booster vaccination concentration ≥ 20 El.U/ml: an increase in antibody concentrations of at least two times the Pre booster vaccination concentration

As with other adult-type Td vaccines, Boostrix Polio induces higher seroprotection rates and higher titres of both anti-D and anti-T antibodies in children and adolescents as compared to adults.

*Persistence of the immune response*

The following seroprotection/seropositivity rates were observed five years after vaccination with Boostrix Polio in children and 10 years after vaccination with Boostrix Polio in adolescents and adults (Table 5).

**Table 5**: Persistence of immune response in children, adolescents and adults

| Antigen | Seroprotection/ seropositivity | Percentages meeting criteria 5 years after vaccination of children (aged 4-8 years) (N=344) (% vaccinees) | Percentages meeting criteria 10 years after vaccination of adolescents and adults (aged 15 years onwards) (N=63) (% vaccinees) |
|---|---|---|---|
| **Diphtheria** | ≥ 0.1 IU/ml | 89.4%* | 81.0%** |
| **Tetanus** | ≥ 0.1 IU/ml | 98.5% | 98.4% |
| **Pertussis** | ≥ 5 EL.U/ml | | |
| Pertussis toxoid | | 40.9% | 78.7% |
| Filamentous haemagglutinin | | 99.7% | 100% |
| Pertactin | | 97.1% | 88.7% |
| **Inactivated poliovirus** | ≥ 8 ED50 | | |
| type 1 | | 98.8% | 100% |
| type 2 | | 99.7% | 100% |
| type 3 | | 97.1% | 98.3% |

*98.2% of subjects with antibody concentrations associated with protection against disease ≥ 0.016 IU/ml by an *in-vitro* Vero-cell neutralisation assay.
**92.1% of subjects with antibody concentrations associated with protection against disease ≥ 0.01 IU/ml by an *in-vitro* Vero-cell neutralisation assay.

*Immune response after a repeat dose*

The immunogenicity of Boostrix-Polio, administered 5 years after a first booster dose of Boostrix-Polio at 4 to 8 years of age, has been evaluated. One month post vaccination, > 99 % of subjects were seropositive against pertussis and seroprotected against diphtheria, tetanus and all three poliovirus types.

In adults, one dose of Boostrix-Polio administered 10 years after the previous dose, elicited a protective immune response in > 96.8% of the subjects (for the diphtheria antigen) and in 100% of the subjects (for the tetanus and polio antigens). The booster response against the pertussis antigens was between 74.2 and 98.4%.

*Immune response in subjects without prior or with unknown vaccination history*

After administration of one dose of Boostrix (dTpa component of Boostrix-Polio) to 83 adolescents aged from 11 to 18 years, without previous pertussis vaccination and no vaccination against diphtheria and tetanus in the previous 5 years, all subjects were seroprotected against tetanus and diphtheria. The seropositivity rate after one dose varied between 87% and 100% for the different pertussis antigens.

After administration of one dose of Boostrix-Polio to 140 adults ≥ 40 years of age (including those who have never been vaccinated or whose vaccination status was unknown), that had not received any diphtheria and tetanus containing vaccine in the past 20 years, more than 96.4% of adults were seropositive for all three pertussis antigens and 77.7% and 95.7% were seroprotected against diphtheria and tetanus respectively.

*Immune response and safety profile in subjects on active treatment for obstructive airway diseases*
The safety and immunogenicity of Boostrix have been evaluated in a descriptive meta-analysis study combining data from 222 subjects ≥ 18 years of age vaccinated with Boostrix while on active treatment for obstructive airway disease such as asthma or Chronic Obstructive Pulmonary Disease (COPD). One month after Boostrix vaccination, the immune responses against diphtheria and tetanus

antigens in terms of seroprotective rates (≥ 0.1 IU/mL) were respectively 89.0% and 97.2%, and against pertussis in terms of booster responses these were 78.3 %, 96.1 % and 92.2 % against pertussis toxoid [PT], filamentous haemagglutinin [FHA] and pertactin [PRN], respectively. These results are consistent with the responses obtained in the general adult population and with a similar safety profile.

*Efficacy in protecting against pertussis*

The pertussis antigens contained in Boostrix Polio are an integral part of the paediatric acellular pertussis combination vaccine (Infanrix), for which efficacy after primary vaccination has been demonstrated in a household contact efficacy study. The antibody titres to all three pertussis components following vaccination with Boostrix Polio are at least as high or higher than those observed during the household contact efficacy trial. Based on these comparisons, Boostrix Polio would provide protection against pertussis, however the degree and duration of protection afforded by the vaccine are undetermined.

*Effectiveness in the protection against pertussis disease in infants born to women vaccinated during pregnancy*

Boostrix or Boostrix-Polio vaccine effectiveness (VE) was evaluated in three observational studies, in UK, Spain and Australia. The vaccine was used during the third trimester of pregnancy to protect infants below 3 months of age against pertussis disease, as part of a maternal vaccination programme.

Details of each study design and results are provided in Table 6.

**Table 6:** VE against pertussis disease for infants below 3 months of age born to mothers vaccinated during the third trimester of pregnancy with Boostrix/Boostrix-Polio

| Study location | Vaccine | Study design | Vaccination Effectiveness |
|---|---|---|---|
| **UK** | *Boostrix-Polio* | Retrospective, screening method | 88% (95% CI: 79, 93) |
| **Spain** | *Boostrix* | Prospective, matched case-control | 90.9% (95% CI: 56.6, 98.1) |
| **Australia** | *Boostrix* | Prospective, matched case-control | 69% (95% CI: 13, 89) |

CI: confidence interval

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

## 5.2 Pharmacokinetic properties

Evaluation of pharmacokinetic properties is not required for vaccines.

## 5.3 Preclinical safety data

**Reproductive toxicology**

*Fertility*

Non-clinical data obtained with Boostrix-Polio reveal no specific hazard for humans based on conventional studies of female fertility in rats and rabbits.

*Pregnancy*

Non-clinical data obtained with Boostrix-Polio reveal no specific hazard for humans based on conventional studies of embryo-foetal development in rats and rabbits, and also of parturition and

postnatal toxicity in rats (up to the end of the lactation period).

**Animal toxicology and/or pharmacology**

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

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Medium 199 (as stabilizer containing amino acids(including phenylalanine), mineral salts(including sodium and potassium), vitamins (including para-aminobenzoic acid) and other substances)
Sodium chloride
Water for injections
Aluminum (as aluminum salt)

For adjuvants, see section 2.

### 6.2 Incompatibilities

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

### 6.3 Shelf life

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

### 6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C).

After first opening, use immediately.

**Do not freeze.**

Store in the original package in order to protect from light.

### 6.5 Nature and contents of container

0.5 ml of suspension in a pre-filled syringe (type I glass) with a plunger stopper (butyl rubber) and with a rubber tip cap.
Pack sizes of 1 and 10, with or without needles.

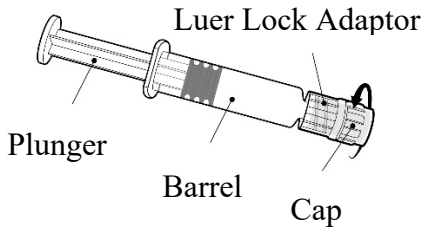
The tip cap and rubber plunger stopper of the pre-filled syringe are made with synthetic rubber.

Not all pack sizes may be marketed.

### 6.6 Special precautions for disposal and other handling

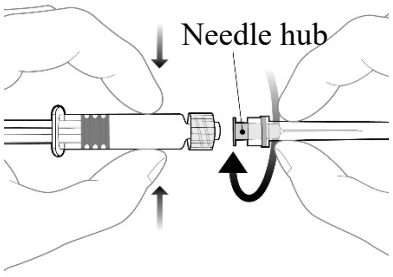
Prior to use, the vaccine should be at room temperature, and well shaken in order to obtain a homogeneous turbid white suspension. Prior to administration, the vaccine should be visually inspected for any foreign particulate matter and/or variation of physical aspect. In the event of either being observed, do not administer the vaccine.

Instructions for the pre-filled syringe




Hold the syringe by the barrel, not by the plunger.

Unscrew the syringe cap by twisting it anticlockwise.




To attach the needle, connect the hub to the Luer Lock Adaptor and rotate a quarter turn clockwise until you feel it lock.

Do not pull the syringe plunger out of the barrel. If it happens, do not administer the vaccine.

Disposal:

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

## 7. MANUFACTURER

GlaxoSmithKline Biologicals S.A., Rixensart, Belgium.

## 8. LICENSE HOLDER AND IMPORTER

GlaxoSmithKline (Israel) Ltd., 25 Basel St., Petach Tikva.

## 9. LICENSE NUMBER

136-97-31449



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Boo IPV DR V9