# Boostrix Polio

**Diphtheria, tetanus, pertussis (acellular, component) and poliomyelitis (inactivated) vaccine (adsorbed, reduced antigen(s) content)**
**Suspension for injection**

## 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 | |

Boostrix Polio is a turbid white suspension. Upon storage, a white deposit and clear supernatant can be observed. This is a normal finding.

## CLINICAL INFORMATION

### Indications

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

The use of Boostrix Polio should be in accordance with official recommendations.

### Dosage and 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. Boostrix Polio should be administered in accordance with official recommendations and/or local practice

regarding the use of vaccines with reduced content of diphtheria toxoid plus tetanus toxoid in combination with pertussis and poliomyelitis antigens.

Boostrix Polio can be administered to pregnant women during the second or the third trimester in accordance with official recommendations (see *Pregnancy* and P*harmacodynamics*).

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 polio (see *Pharmacodynamics*). 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.

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. 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 (generally 10 years).

### Method of administration

Boostrix Polio is for deep intramuscular injection, preferably in the deltoid region (see also *Warnings and Precautions*).

## Contraindications

Boostrix Polio should not be administered to subjects with known hypersensitivity to any component of the vaccine (see *Quantitative and Qualitative composition* and *List of Excipients*) or to subjects having shown signs of 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 neurological complications following an earlier immunisation against diphtheria and/or tetanus (for convulsions or hypotonic-hyporesponsive episodes, see *Warnings and Precautions*).

## Warnings and Precautions

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.

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.

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.

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

- Temperature of ≥ 40.0°C (rectal) within 48 hours of vaccination, not due to another identifiable cause.
- Collapse or shock-like state (hypotonic-hyporesponsive 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, particularly since these events are not associated with permanent sequelae. According to available clinical data, the risk of such reactions is lower with acellular pertussis vaccines than with whole cell pertussis vaccines.

In children with progressive neurological disorders, including infantile spasms, uncontrolled epilepsy or progressive encephalopathy, it is better to defer pertussis (Pa or Pw) immunisation until the condition is corrected or stable. However, the decision to give pertussis vaccine must be made on an individual basis after careful consideration of the risks and benefits.

**Boostrix Polio should in no circumstances be administered intravascularly.**

Boostrix Polio should be administered with caution to subjects with thrombocytopenia 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.

Collapse or shock-like state (hypotonic-hyporesponsive episode) and convulsions have been reported very rarely following immunisation of children with products containing one or more of the antigenic constituents of Boostrix Polio.

A history of febrile convulsions, a family history of convulsions, a family history of Sudden Infant Death Syndrome (SIDS) 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, e.g. patients on immunosuppressive therapy.

Syncope (fainting) can occur following, or even before, any vaccination as a psychogenic response to the needle injection. 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.

## Interactions

Boostrix Polio can be given concomitantly with any of the following monovalent or combination vaccines: measles, mumps, rubella, varicella and human papilloma virus vaccine (see *Adverse Reactions*).

The sequential administration of combined dTpa-IPV followed by Cervarix one month later tended to elicit lower anti-HPV-16 and anti-HPV-18 GMTs compared to Cervarix alone. The clinical relevance of this observation is not known.

Concomitant use with other inactivated vaccines and with immunoglobulin is unlikely to result in interference with the immune responses.

If Boostrix Polio is to be given at the same time as another injectable vaccine or immunoglobulin, the products should always be given at different sites.

As with other vaccines, it may be expected that in patients receiving immunosuppressive therapy or patients with immunodeficiency an adequate immunologic response may not be achieved.

## Pregnancy and Lactation

### Fertility

No human data available. Animal studies do not indicate direct or indirect harmful effects with respect to female fertility.

### Pregnancy

Boostrix Polio can be used during the second or third trimester of pregnancy in accordance with official recommendations.

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

Safety data from a randomised controlled clinical trial (341 pregnancy outcomes) and from a prospective observational study (793 pregnancy outcomes) where Boostrix (dTpa component of Boostrix Polio) was administered to pregnant women during the third trimester have shown no vaccine related adverse effect on pregnancy or on the health of the foetus/newborn child.

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

Data from post-marketing surveillance where pregnant women were exposed to Boostrix Polio or to Boostrix in the second or the third trimester have shown no vaccine related adverse effect on pregnancy or on the health of the foetus/newborn child.

As with other inactivated vaccines, it is not expected that vaccination with Boostrix Polio harms the foetus at any trimester of pregnancy.

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

### Lactation

The safety of Boostrix Polio when administered to breast-feeding women has not been evaluated.

It is unknown whether Boostrix Polio is excreted in human breast milk.

Boostrix Polio should only be used during breast-feeding when the possible advantages outweigh the potential risks.

## Effects on Ability to Drive and Use Machines

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

## Adverse Reactions

### Clinical Trial Data

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 9 years of age) and 955 adults, adolescents and children (above 10 years of age). The most common events occurring after vaccine administration in both groups were local injection site reactions (pain, redness and swelling) reported by 31.3 – 82.3% of subjects overall. These had their onset within the first day after vaccination. All resolved without sequelae.

Adverse reactions reported are listed according to the following frequency:

| | |
|---|---|
| Very common | ≥1/10 |
| Common | ≥1/100 and <1/10 |
| Uncommon | ≥1/1000 and <1/100 |
| Rare | ≥1/10,000 and <1/1000 |
| Very rare | <1/10,000 |

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

| ***System Organ Class*** | ***Frequency*** | ***Adverse reactions*** | |
|---|---|---|---|
| | | ***Children from 4 to 9 years of age*** | ***Adults, adolescents and children from the age of 10 years onwards*** |
| ***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 |

| | | | |
|---|---|---|---|
| | Uncommon | diarrhoea, vomiting, abdominal pain, nausea | |
| ***Skin and subcutaneous tissue disorders*** | Uncommon | | pruritus |
| ***Musculoskeletal and connective tissue disorders*** | Uncommon | | myalgia, arthralgia |
| ***General disorders and administration site conditions*** | Very common | injection site reactions (including pain, redness and swelling) | injection site reactions (including pain, redness and swelling), fatigue |
| | Common | fever ≥ 37.5 °C (including fever > 39°C), injection site reactions (such as haemorrhage) | fever ≥ 37.5 °C, injection site reactions (such as haematoma) |
| | Uncommon | fatigue | fever > 39 °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 9 years of age) and 1931 adults, adolescents and children (above 10 years of age), are listed in Table 2:

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

| ***System Organ Class*** | ***Frequency*** | ***Adverse reactions*** | |
|---|---|---|---|
| | | ***Children from 4 to 9 years of age*** | ***Adults, adolescents and children from the age of 10 years onwards*** |
| ***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*** | Common | | nausea |
| | Uncommon | | diarrhoea, vomiting |
| ***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 | injection site reactions (such as induration), pain | influenza like illness |

*Reactogenicity after repeat dose of Boostrix Polio or Boostrix*

Subjects fully primed with 4 doses of DTPa followed by Boostrix Polio at around 4-8 years of age show no increased reactogenicity after the second Boostrix Polio dose administered 5 years later.

Subjects aged 15 years onwards without recent vaccination for diphtheria, tetanus, pertussis and polio, 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.

Subjects fully primed with 4 doses of DTPw followed by a Boostrix dose around 10 years of age show an increase of local reactogenicity after an additional Boostrix dose administered 10 years later.

### Post Marketing Data

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

| *System Organ Class* | *Frequency* | *Adverse reactions* |
|---|---|---|
| ***Blood and lymphatic system disorders*** | Rare | angioedema |
| ***Immune system disorders*** | Very rare | allergic reactions, including anaphylactic and anaphylactoid reactions |
| ***Nervous system disorders*** | Rare | convulsions (with or without fever) |
| ***Skin and subcutaneous tissue disorders*** | Rare | urticaria |
| ***General disorders and administration site conditions*** | Rare | extensive swelling of the vaccinated limb, asthenia |

## 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.

# PHARMACOLOGICAL PROPERTIES

## Pharmacodynamics

Pharmaco-therapeutic group: Bacterial and viral vaccines combined, ATC code J07CA02

*Immune response*

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 9 years** N=1195 (% vaccinees) | **Adults, adolescents and children aged from 10 years onwards** N=923 (% vaccinees) |
|---|---|---|---|
| **Diphtheria** | ≥ 0.1 IU/ml | 100% | 82.2 – 100% |
| **Tetanus** | ≥ 0.1 IU/ml | 99.9 – 100% | 99.6 – 100% |
| **Pertussis** | Booster response* | | |
| 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

*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.

*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.

*Immunogenicity against pertussis antigens in infants (below 3 months of age) born to mothers vaccinated during pregnancy.*

In a randomised, cross-over, placebo-controlled study, higher pertussis antibody concentrations were demonstrated at delivery in the cord blood of babies born to mothers vaccinated with Boostrix (N=291) versus placebo (N=292) during the third trimester of pregnancy. The cord blood geometric mean concentrations of antibodies against the pertussis antigens PT, FHA and PRN were 46.9, 366.1 and 301.8 IU/ml in the dTpa group, and 5.5, 22.7 and 14.6 IU/ml in the control group. This corresponds to concentrations of antibodies against the pertussis antigens PT, FHA and PRN that are respectively 8, 16 and 21 times higher in the cord blood of babies born to vaccinated mothers versus controls. These antibody titres may provide passive protection against pertussis, as shown by observational effectiveness studies.

*Immunogenicity in infants and toddlers born to mothers vaccinated during pregnancy*

The immunogenicity of Infanrix hexa in infants and toddlers born to health mothers vaccinated with dTpa at 27-36 weeks of pregnancy was evaluated in two clinical studies.

Infanrix hexa was co-administered with 13-valent pneumococcal conjugate vaccine to infants at 2, 4 and 6 months or 2, 3 and 4 months in three-dose primary vaccination schedules (n=241), or at 3 and 5 months or 2 and 4 months in two-dose primary vaccination schedules (n=27) and to the same infants/toddlers from 11 to 18 months as booster dose (n=229).

Post-primary and post-booster vaccination, immunological data did not show clinically relevant interference of maternal vaccination with dTpa on the infant's and toddler's responses to diphtheria, tetanus, hepatitis B, inactivated poliovirus, *Haemophilus influenzae* type b or pneumococcal antigens.

For diphtheria, at the pre-booster timepoint 81.2% of infants in the dTpa Group and 90.2% in the Control Group were seroprotected. Post-booster vaccination, all subjects in both study groups were seroprotected.

Lower antibody concentrations against pertussis antigens post-primary (PT, FHA and PRN) and post-booster (PT, FHA) vaccination were observed in infants and toddlers born to mothers vaccinated with dTpa during pregnancy. The fold-increases of anti-pertussis antibody concentrations from the pre-booster to the 1-month post-booster time point were in the same range for infants and toddlers born to mothers vaccinated with dTpa or with placebo, demonstrating effective priming of the immune system. In the absence of correlates of protection for pertussis, the clinical relevance of these observations remains to be fully understood. However, current epidemiological data on pertussis disease following the implementation of dTpa maternal immunisation do not suggest any clinical relevance of this immune interference.

*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 5.

**Table 5:** 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.

*Persistence of the immune response*

Five years following vaccination with Boostrix Polio, at least 89.4% of children from the age of 4 to 8 years were seroprotected or seropositive against all vaccine components, except for the pertussis toxoid component (40.9% of subjects were seropositive against pertussis toxoid).

Ten years following vaccination with Boostrix Polio, at least 78.7% of adults and adolescents were seroprotected or seropositive against all vaccine components.

*Immune response after a repeat dose of Boostrix Polio*

The immunogenicity of Boostrix Polio, administered 5 years after a previous 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 polio 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*

In adolescents aged from 11 to 18 years, without previous pertussis vaccination and no vaccination against diphtheria and tetanus in the previous 5 years, one dose of Boostrix (dTpa component of Boostrix Polio) induced an antibody response against pertussis and all subjects were protected against tetanus and diphtheria.

In subjects ≥ 40 years of age that had not received any diphtheria or tetanus containing vaccine in the past 20 years (including those who have never been vaccinated or whose vaccination status was unknown), one dose of Boostrix Polio induced an antibody response against pertussis and protected against tetanus and diphtheria in the majority of cases.

## Pre-clinical Safety Data

### Animal toxicology and/or pharmacology

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

# PHARMACEUTICAL INFORMATION

## List of Excipients

Medium 199 (as stabilizer), sodium chloride, water for injections.
Neomycin sulphate, polymyxin B sulphate are present as residues from the manufacturing process.

## Shelf Life

The expiry date is indicated on the label and packaging.

## Storage

Store in a refrigerator (2°C – 8°C).

**Do not freeze**. Discard if the vaccine has been frozen.

Protect from light.

The storage conditions are detailed on the packaging.

## 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 not made with natural rubber latex.

Not all presentations are available in every country.

## Incompatibilities

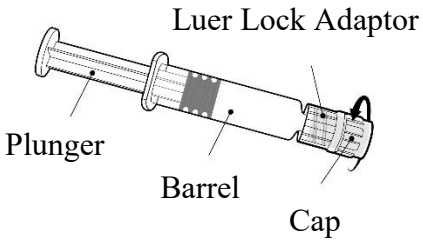
Boostrix Polio should not be mixed with other vaccines in the same syringe.

## Use and 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.

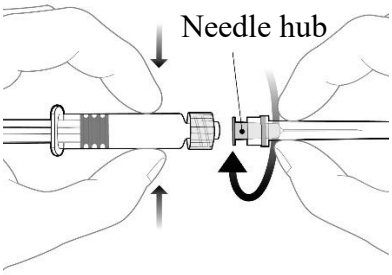
Upon removal from refrigerator, the vaccine is stable for 8 hours at + 21°C.

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



## Product Owner:

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