Summary of Product Characteristic (SmPC)

▼**This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See Section 4.8 for how to report adverse reactions.**

1. NAME OF THE MEDICINAL PRODUCT

VaxigripTetra, suspension for injection in pre-filled syringe

Quadrivalent influenza vaccine (split virion, inactivated)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Influenza virus (inactivated, split) of the following strains*:

A/California/7/2009 (H1N1)pdm09 - like strain (A/California/7/2009, NYMC X-179A)..... .....15 micrograms HA**

A/Texas/50/2012 (H3N2) - like strain (A/Texas/50/2012, NYMC X-223A)..... .....15 micrograms HA**

B/Massachusetts/2/2012 (Yamagata lineage).....15 micrograms HA**

B/Brisbane/60/2008 (Victoria lineage).....15 micrograms HA**

Per 0.5 ml dose

* propagated in fertilised hens' eggs from healthy chicken flocks

** haemagglutinin

This vaccine complies with the WHO recommendations (Northern hemisphere) and EU decision for the 2014/2015 season.

For the full list of excipients, see Section 6.1.

VaxigripTetra may contain traces of eggs, such as ovalbumin, and of neomycin, formaldehyde and octoxinol-9, which are used during the manufacturing process (see Section 4.3).

3. PHARMACEUTICAL FORM

Suspension for injection in pre-filled syringe.

The vaccine, after shaking gently, is a colourless opalescent liquid.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

VaxigripTetra is indicated for active immunisation of adults and children from 6 months of age and older for the prevention of influenza disease caused by the two influenza A virus subtypes and the two influenza B virus types contained in the vaccine.

The use of VaxigripTetra should be based on official recommendations.

4.2 Posology and method of administration

Posology

Based on clinical experience with the trivalent vaccine, annual revaccination with influenza vaccine is recommended given the duration of immunity provided by the vaccine and because circulating strains of influenza virus might change from year to year.

Adults: one dose of 0.5 ml.

Paediatric population

- Children from 6 months to 17 years of age: one dose of 0.5 ml.
  For children less than 9 years of age who have not previously been vaccinated, a second dose of 0.5 ml should be given after an interval of at least 4 weeks.

- Children less than 6 months of age: the safety and efficacy of VaxigripTetra have not been established. No data are available.

Method of administration

The vaccine should be given by intramuscular or subcutaneous injection.

The preferred sites for intramuscular injection are the anterolateral aspect of the thigh (or the deltoid muscle if muscle mass is adequate) in children 6 months through 35 months of age, or the deltoid muscle in children from 36 months of age and adults.

Precautions to be taken before handling or administering the medicinal product

For instructions on preparation of the medicinal product before administration, see Section 6.6.

4.3 Contraindications

Hypersensitivity to the active substances, to any of the excipients listed in Section 6.1 or to any component that may be present as traces such as eggs (ovalbumin, chicken proteins), neomycin, formaldehyde and octoxinol-9.

Vaccination should be postponed in case of moderate or severe febrile disease or acute disease.

4.4 Special warnings and precautions for use

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

VaxigripTetra should under no circumstances be administered intravascularly.

As with other vaccines administered intramuscularly, the vaccine should be administered with caution to subjects with thrombocytopaenia or a bleeding disorder since bleeding may occur following an intramuscular administration to these subjects.

Syncope (fainting) can occur following, or even before, any vaccination as a psychogenic response to the needle injection. Procedures should be in place to prevent injury from fainting and manage syncopal reactions.

VaxigripTetra is intended to provide protection against those strains of influenza virus from which the vaccine is prepared.

As with any vaccine, vaccination with VaxigripTetra may not protect all vaccinees.

Antibody response in patients with endogenous or iatrogenic immunosuppression may be insufficient.

Interference with serological testing

See Section 4.5.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed with VaxigripTetra.

VaxigripTetra can be given at the same time as other vaccines, based on clinical experience with Vaxigrip. Separate injection sites and separate syringes should be used in case of concomitant administration.

The immunological response may be reduced if the patient is undergoing immunosuppressant treatment.

Following influenza vaccination, false positive results in serology tests using the ELISA method to detect antibodies against HIV1, Hepatitis C and especially HTLV1 have been observed. The Western Blot

technique disproves the false-positive ELISA test results. The transient false positive reactions could be due to the IgM response by the vaccine.

4.6 Fertility, pregnancy and lactation

Pregnancy

Inactivated influenza vaccines can be used in all stages of pregnancy. Larger datasets on safety are available for the second and third trimester, compared with the first trimester; however, data from worldwide use of inactivated influenza vaccines do not indicate any adverse foetal and maternal outcomes attributable to the vaccine.

There are no data on the use of VaxigripTetra in pregnant women.

One animal study with VaxigripTetra did not indicate direct or indirect harmful effects with respect to pregnancy, embryo-foetal development or early post-natal development

Breastfeeding

VaxigripTetra may be used during breastfeeding.

Fertility

There are no fertility data available in Humans. One animal study with Vaxigrip etra did not indicate harmful effects on female fertility.

4.7 Effects on ability to drive and use machines

VaxigripTetra has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

a. Summary of the safety profile

The safety of VaxigripTetra was assessed in six clinical trials in which 3,040 adults from 18 to 60 years of age, 1,392 elderly over 60 years of age and 429 children from 9 to 17 years of age received one dose of VaxigripTetra and 884 children from 3 to 8 years of age received one or two doses of VaxigripTetra depending on their influenza vaccination history and 1,614 children from 6 to 35 months of age received two doses (0.5 ml) of VaxigripTetra.

Most reactions usually occurred within the first 3 days following vaccination, resolved spontaneously within 1 to 3 days after onset. The intensity of these reactions was mild.
The most frequently reported adverse reaction after vaccination, in all populations including the whole group of children from 6 to 35 months of age, was injection site pain (between 52.8% and 56.5% in children from 3 to 17 years of age and in adults, 26.8% in children from 6 to 35 months of age and 25.8%

in elderly). In subpopulation of children less than 24 months of age, irritability (32.3%) was the most frequently reported adverse reaction.

In subpopulation children from 24 to 35 months of age, malaise (26.8%) is the most frequently reported adverse reaction.

The other most frequently reported adverse reactions after vaccination were:

- In adults: headache (27.8%), myalgia (23%) and malaise (19.2%),
- In elderly: headache (15.6%) and myalgia (13.9%),
- In children from 9 to 17 years of age: myalgia (29.1%), headache (24.7%), malaise (20.3%) and injection site swelling (10.7%),
- In children from 3 to 8 years of age: malaise (30.7%), myalgia (28.5%), headache (25.7%), injection site swelling (20.5%), injection site erythema (20.4%), injection site induration (16.4%), shivering (11.2%),
- For all children from 6 to 35 months: fever (20.4%) and injection site erythema (17.2%),
- In children less than 24 months: appetite lost (28.9%), crying abnormal (27.1%), vomiting (16.1%) and drowsiness (13.9%),
- In children from 24 months to 35 months: headache (11.9%) and myalgia (11.6%).
- Overall, adverse reactions were generally less frequent in the elderly than in adults and children.

b. Tabulated summary of adverse reactions

The data below summarize the frequencies of the adverse reactions that were recorded following vaccination with VaxigripTetra during clinical trials.

Adverse events are ranked under headings of frequency using the following convention:

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).

Adult and elderly

The safety profile presented below is based on data from 3,040 adults from 18 to 60 years of age and 1,392 elderly over 60 years of age.

ADVERSE REACTIONS	FREQUENCY
Blood and Lymphatic System Disorders	
Lymphadenopathy [(1)]	Uncommon
Immune System Disorders	
Hypersensitivity [(1)], allergic reactions such as erythema, urticaria [(1)], pruritus [(2)], pruritus generalised [(1)], dermatitis allergic [(1)], angioedema [(1)]	Rare
Nervous System Disorders	
Headache	Very common
Dizziness [(3)]	Uncommon
Somnolence, paraesthesia	Rare
Vascular disorders	
Hot flush [(4)]	Uncommon
Respiratory, thoracic and mediastinal disorders	
Dyspnoea [(1)]	Rare
Gastrointestinal Disorders	
Diarrhoea, nausea [(5)]	Uncommon
Skin and Subcutaneous System Disorders	
Hyperhidrosis	Rare
Musculoskeletal and Connective Tissue Disorders	
Myalgia	Very common
Arthralgia [(1)]	Rare
General Disorders and Administration Site Conditions	
Malaise [(6)] Injection site pain	Very common
Shivering, fever [(2)] Injection site erythema, injection site swelling, injection site induration	Common

ADVERSE REACTIONS	FREQUENCY
Fatigue Injection site ecchymosis, injection site pruritus, injection site warmth	Uncommon
Asthenia, flu-like illness Injection site discomfort [(1)]	Rare

[(1)] In adults [(2)] Uncommon in elderly [(3)] Rare in adults [(4)] In elderly

[(5)] Rare in elderly [(6)] Common in elderly

Paediatric population

The safety profile presented below is based on data from 429 children from 9 to 17 years of age who received one dose of VaxigripTetra and from 884 children from 3 to 8 years of age who received one or two doses of VaxigripTetra depending on their influenza vaccination history.

ADVERSE REACTIONS	FREQUENCY
Blood and Lymphatic System Disorders	
Thrombocytopaenia [(1)]	Uncommon
Psychiatric disorders	
Moaning [(2)], restlessness [(2)]	Uncommon
Nervous System Disorders	
Headache	Very common
Dizziness [(2)]	Uncommon
Gastrointestinal Disorders	
Diarrhoea, vomiting [(2)], abdominal pain upper [(2)]	Uncommon
Musculoskeletal and Connective Tissue Disorders	
Myalgia	Very common
Arthralgia [(2)]	Uncommon
General Disorders and Administration Site Conditions	
Malaise, shivering [(3)]	Very common

Injection site pain, injection site swelling, injection site erythema [3], injection site induration [3]	
Fever Injection site ecchymosis	Common
Fatigue [2], Injection site warmth [2], injection site pruritus [4]	Uncommon

[1] Reported in one child of 3 years of age

[2] Reported in children from 3 to 8 years of age

[3] Common in children from 9 to 17 years of age

[4] Reported in children from 9 to 17 years of age

The safety profile presented below is based on data from 1,614 children from 6 to 35 months who received two doses of VaxigripTetra.

ADVERSE REACTIONS	FREQUENCY
Immune System Disorders	
Hypersensitivity	Uncommon
Allergic reactions such as pruritus generalised, rash papular	Rare
Nervous System Disorders	
Headache [1]	Very common
Gastrointestinal Disorders	
Vomiting [2]	Very common
Diarrhoea	Uncommon
Musculoskeletal and Connective Tissue Disorders	
Myalgia [3]	Very common
General Disorders and Administration Site Conditions	
Irritability [4], appetite lost [4], crying abnormal [5], malaise [3], fever, drowsiness [5], injection site pain/tenderness, injection site erythema	Very common
Shivering [1] Injection site induration, injection site swelling, injection site ecchymosis	Common
Injection site rash, injection site pruritus , influenza like illness	Rare

[(1)] Reported in children ≥24 months of age

[(2)] Uncommon in children ≥24 months of age

[(3)] Rare in children <24 months of age

[(4)] Rare in children ≥24 months of age

[(5)] Reported in children <24 months of age

In children from 6 months to 8 years of age, the safety profile of VaxigripTetra was similar after the first and the second injections with a trend of lower incidence of adverse reactions after the second injection compared to the first one in children from 6 to 35 months.

c. Potential adverse events

There are no safety data from post-marketing experience with VaxigripTetra.

However, the following adverse reactions have been reported with Vaxigrip during clinical trials or from post-marketing experience and may occur in people receiving VaxigripTetra.

- ***Immune system disorders***

Severe allergic reactions: shock

Allergic reactions: rash, generalized erythema

- ***Nervous system disorders***

Guillain-Barré Syndrome (GBS), neuritis, neuralgia, convulsions, encephalomyelitis

- ***Vascular disorders***

Vasculitis, such as Henoch-Schönlein purpura, with transient renal involvement in certain cases

d. Other special populations

The safety profile of VaxigripTetra observed in a limited number of subjects with co-morbidities enrolled in the clinical studies does not differ from the one observed in the overall population. In addition, studies conducted with Vaxigrip in renal transplant patients, and asthmatic patients showed no major differences in terms of safety profile of Vaxigrip in these populations.

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.

4.9 Overdose

Not documented for VaxigripTetra. Cases of administration of more than the recommended dose (overdose) have been reported with Vaxigrip. When adverse reactions were reported, the information was consistent with the known safety profile of Vaxigrip.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Influenza vaccine, ATC code: J07BB02.

Mechanism of action

VaxigripTetra provides active immunisation against four influenza virus strains (two A subtypes and two B types) contained in the vaccine.

VaxigripTetra induces humoral antibodies against the haemagglutinins within 2 to 3 weeks. These antibodies neutralise influenza viruses.

Specific levels of haemagglutination-inhibition (HAI) antibody titer post-vaccination with inactivated influenza virus vaccines have not been correlated with protection from influenza illness but the HAI antibody titers have been used as a measure of vaccine activity. In some human challenge studies, HAI antibody titers of ≥1:40 have been associated with protection from influenza illness in up to 50% of subjects.

Since influenza viruses constantly evolve, the virus strains selected in the vaccine are reviewed annually by the WHO.

Annual revaccination with VaxigripTetra has not been studied. However, based on clinical experience with the trivalent vaccine, annual influenza vaccination is recommended given the duration of immunity provided by the vaccine and because circulating strains of influenza virus change from year to year.

Efficacy of VaxigripTetra

Paediatric population

- Children aged from 6 to 35 months:

A randomized placebo controlled study was conducted in 4 regions (Africa, Asia, Latina America and Europe) over 4 influenza seasons, in more than 5,400 children from 6 to 35 months of age who received two doses (0.5 ml) of VaxigripTetra (N=2,722), or placebo (N=2,717) 28 days apart to assess VaxigripTetra efficacy for the prevention of influenza illness laboratory-confirmed by reverse transcriptase polymerase chain reaction (RT-PCR) and/or viral culture caused by strain A and/or B and caused by vaccine similar strains (as determined by sequencing).

ILI was defined as occurrence of fever ≥ 38°C (that lasts at least 24 hours) concurrently with at least one of the following symptoms: cough, nasal congestion, rhinorrhoea, pharyngitis, otitis, vomiting, or diarrhoea.

Table 1: Influenza Attack Rates and VaxigripTetra Efficacy against laboratory-confirmed influenza illness in children from 6 to 35 months of age

	VaxigripTetra (N=2,584)		Placebo (N=2,591)		Efficacy
	n	Influenza Attack Rate (%)	n	Influenza Attack Rate (%)	% (2-sided 95% CI)
Laboratory-confirmed influenza illness caused by:					
- Any influenza A or B type	122	4.72	255	9.84	52.03 (40.24; 61.66)
- Viral strains similar to those contained in the vaccine	26	1.01	85	3.28	69.33 (51.93; 81.03)

N: Number of children analysed (full set)

n: number of subjects fulfilling the item listed

In addition, a predefined complementary analysis showed VaxigripTetra prevented 56.6% (95% CI: 37.0; 70.5) of severe laboratory-confirmed influenza illnesses due to any strain, and 71.7% (95% CI: 43.7; 86.9) of severe laboratory-confirmed influenza illnesses due to vaccine-similar strains. Furthermore, subjects receiving VaxigripTetra were 59.2% (95% CI: 44.4; 70.4) less likely to experience a medically attended influenza illness than subjects receiving placebo.
Severe laboratory-confirmed influenza illnesses was defined as ILI laboratory-confirmed by RT-PCR and/or Viral culture with at least one of the following items:

- fever > 39.5°C for subjects aged < 24 months or ≥ 39.0°C for subjects aged ≥ 24 months,
- and/or at least one significant ILI symptom which prevents daily activity (cough, nasal congestion, rhinorrhoea, pharyngitis, otitis, vomiting, diarrhoea),
- and/or one of the following events: acute otitis media, acute lower respiratory infection (pneumonia, bronchiolitis, bronchitis, croup), inpatient hospitalization.

- Children from 3 to 8 years of age:

Based on immune responses observed in children 3 to 8 years of age, the efficacy of VaxigripTetra in this population is expected to be at least similar to the efficacy observed in children from 6 to 35 months (see “Children from 6 to 35 months of age ” above and “Immunogenicity of VaxigripTetra“ below).

Immunogenicity of VaxigripTetra

Clinical studies performed in adults from 18 to 60 years of age, in elderly over 60 years of age, in children from 3 to 8 years of age and from 6 to 35 months of age assessed VaxigripTetra immune response for HAI

Geometric mean antibody titer (GMT) at Day 21 (for adults) and at Day 28 (for children), HAI seroconversion rate (4-fold rise in reciprocal titer or change from undetectable [< 10] to a reciprocal titer of ≥ 40), and HAI GMTR (post-/pre-vaccination titers).

One clinical study performed in adults from 18 to 60 years of age and in children from 9 to 17 years of age described the immune response of VaxigripTetra for HAI Geometric mean antibody titer (GMT) at Day 21. Another clinical study performed in children from 9 to 17 years of age described the immune response of VaxigripTetra.

VaxigripTetra induced a significant immune response to the 4 influenza strains contained in the vaccine.

Adults and elderly

A total of 832 adults from 18 to 60 years of age and 831 elderly over 60 years of age were assessed in terms of immune response after one dose of VaxigripTetra.

Immunogenicity results are presented in the table below:

Table 2: Immunogenicity results in adults aged from 18 to 60 years and in elderly over 60 years of age

Antigen Strain	18 to 60 years of age N=832	over 60 years of age N=831
GMT (95% CI)		
A (H1N1) [(a)(b)]	608 (563;657)	219 (199; 241)
A (H3N2)	498 (459; 541)	359 (329; 391)
B (Victoria)	708 (661; 760)	287 (265; 311)
B (Yamagata)	1,715 (1607; 1830)	655 (611; 701)
SC % (95% CI) [(c)]		
A (H1N1) [(a)(b)]	64.1 (60.7; 67.4)	45.6 (42.1; 49.0)
A (H3N2)	66.2 (62.9; 69.4)	47.5 (44.1; 51.0)
B (Victoria)	70.9 (67.7; 74.0)	45.2 (41.8; 48.7)
B (Yamagata)	63.7 (60.3;67.0)	42.7 (39.3; 46.2)
GMTR (95% CI) [(d)]		

A (H1N1) [(a)(b)]	9.77 (8.69; 11.0)	4.94 (4.46; 5.47)
A (H3N2)	10.3 (9.15; 11.5)	5.60 (5.02; 6.24)
B (Victoria)	11.6 (10.4; 12.9)	4.61 (4.18; 5.09)
B (Yamagata)	7.35 (6.66;8.12)	4.11 (3.73; 4.52)

N=number of subjects with available data for the considered endpoint

GMT: Geometric Mean Titer; GMTR: Geometric Mean Titer Ratio; CI: Confidence Interval; SC: Seroconversion; SI: Significant Increase

(a) N=833 for 18-60 years of age group

(b) N=832 for over 60 years of age group

(c) For subjects with a pre-vaccination titer <10 (1/dil), proportion of subjects with a post-vaccination titer ≥40 (1/dil) and for subjects with a pre-vaccination titer ≥10 (1/dil), proportion of subjects with a ≥four-fold increase from pre- to post-vaccination titer

(d) Geometric mean of individual ratios (post-/pre-vaccination titers)

Paediatric population

- Children from 9 to 17 years of age:

In a total of 429 children from 9 to 17 years of age who received one dose of VaxigripTetra, the immune response against the 4 strains contained in the vaccine was similar to the immune response induced in adults from 18 to 60 years of age.

- Children from 6 months to 8 years of age:

A total of 863 children from 3 to 8 years of age received either one or two doses of VaxigripTetra or Vaxigrip depending on their previous influenza vaccination history.

Children who received a one- or two-dose schedule of VaxigripTetra presented a similar immune response following the last dose of the respective schedule.

In addition to the VaxigripTetra efficacy, the immunogenicity of two 0.5 ml-dose of VaxigripTetra was assessed 28 days after receipt of the last injection of VaxigripTetra by HAI method in 341 children 6 to 35 months of age.

Immunogenicity results are presented in the table below:

Table 3: Immunogenicity results in children aged from 6 months to 8 years

Antigen Strain	6-35 month of age N=341	3-8 years of age N=863
GMT (95% CI)		
A (H1N1)	641 (547; 752)	971 (896; 1,052)
A (H3N2)	1,071 (925; 1,241)	1,568 (1,451; 1,695)
B (Victoria)	623 (550; 706)	1,050 (956; 1,154)
B (Yamagata) [(a)]	1,010 (885; 1,153)	1,173 (1,078; 1,276)
SC % (95% CI) [(b)]		
A (H1N1)	90.3 (86.7; 93.2)	65.7 (62.4; 68.9)
A (H3N2)	90.3 (86.7; 93.2)	64.8 (61.5; 68.0)
B (Victoria)	98.8 (97.0; 99.7)	84.8 (82.3; 87.2)
B (Yamagata) [(a)]	96.8 (94.3; 98.4)	88.5 (86.2; 90.6)
GMTR (95% CI) [(c)]		
A (H1N1)	36.6 (30.8; 43.6)	6.86 (6.24; 7.53)
A (H3N2)	42.6 (35.1; 51.7)	7.49 (6.72; 8.35)
B (Victoria)	100 (88.9; 114)	17.1 (15.5; 18.8)
B (Yamagata) [(a)]	93.9 (79.5; 111)	25.3 (22.8; 28.2)

N=number of subjects with available data for the considered endpoint

GMT: Geometric Mean Titer; GMTR: Geometric Mean Titer Ratio; CI: Confidence Interval; SC: Seroconversion; SI: Significant Increase

(a) N=862 for for 3-8 years of age group

(b) For subjects with a pre-vaccination titer <10 (1/dil), proportion of subjects with a post-vaccination titer ≥40 (1/dil) and for subjects with a pre-vaccination titer ≥10 (1/dil), proportion of subjects with a ≥four-fold increase from pre- to post-vaccination titer

(c) Geometric mean of individual ratios (post-/pre-vaccination titers)

These immunogenicity data provide supportive information in addition to vaccine efficacy data available in this population (see Efficacy of VaxigripTetra).

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Non-clinical data revealed no special hazard for humans based on conventional studies of repeat dose and local toxicity, reproductive and developmental toxicity and safety pharmacology studies.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Buffer Solution:

- Sodium chloride
- Potassium chloride
- Disodium phosphate dihydrate
- Potassium dihydrogen phosphate
- Water for injections

6.2 Incompatibilities

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

6.3 Shelf life

1 year

6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C). Do not freeze. Keep the syringe in the outer carton in order to protect from light.

6.5 Nature and contents of container

0.5 ml of suspension in pre-filled syringe (type I glass) with attached needle, equipped with a plunger stopper (elastomer chlorobutyl or bromobutyl) – pack size of 1, 10 or 20.

0.5 ml of suspension in pre-filled syringe (type I glass) without needle, equipped with a plunger stopper (elastomer chlorobutyl or bromobutyl) – pack size of 1, 10 or 20.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

The vaccine should be allowed to reach room temperature before use.

Shake before use. Inspect visually prior to administration.

The vaccine should not be used if foreign particles are present in the suspension.

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

7. MARKETING AUTHORISATION HOLDER

Sanofi Pasteur Ltd., Bangkok

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 11 August 2016

10. DATE OF REVISION OF THE TEXT

26 October 2017